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American Journal of Diseases of Children

VOLUME 47 JANUARY, 1934 NUMBER 1

TREATMENT OF ANEMIA IN CHILDREN

WITH FERRIC AND FERROUS COMPOUNDS, REDUCED IRON AND CUPRIC SULPHATE

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COPENHAGEN, DENMARK

The treatment of patients with iron compounds is of very old date, but its value is still much disputed. Bunge, for instance, was of the opinion that the effect of iron compounds on chlorosis was suggestive. Iron has at times been administered in inorganic compounds, at times in organic ones and at other times as reduced iron. Later years have brought several new points of view, based on clinical and experimental investigations. Ferrous compounds are more effective in chlorosis than ferric compounds. Heubner was of the opinion that patients with chlorosis are not able to convert the trivalent iron of the food to the divalent form of hemoglobin. Amatsu [1] proved that ferrous tartrate, administered intravenously, is far more poisonous than ferric tartrate, and also that it is far more effective in animals with anemia after hemorrhage. Later Starkenstein and his collaborators,[2] who assume that a substance is effective only when larger doses cause poisoning, showed that the only group of iron salts with an effect after absorption are the ferrous salts, while ferric salts precipitate the proteins, and the complex and inorganic compounds do not act as iron, but in union with the rest of the atoms together with which they have formed their compounds. Henriques and Okkels [3] have found deviations in principle between those iron compounds which are able to give off iron ions—the iron being deposited in the reticulo-endothelial system—and the complex iron salts. They have demonstrated a secondary iron poisoning, appearing from four to six months after the intravenous administration of an ionized iron compound, a poisoning which does not appear after treatment with a complex iron compound. Simultaneous with the poisoning, the depots in the reticulo-endothelial system decrease, the iron being deposited in the spleen in compounds which it seems impossible to mobilize. It is not yet known how iron circulates and operates in the organism.

From the University Pediatric Clinic, Rigshospitalet; Chief, Prof. C. E. Bloch.

1. Amatsu: Arch. internat. de pharmacod. **23**:325, 1913.

2. Starkenstein, E., and Weden, H.: Arch. f. exper. Path. u. Pharmakol. **134**:274 and 300, 1928.

3 Henriques, V., and Okkels, H.: Ztschr. f. Zellforsch. u. mikr. Anat. **12**:155, 1930. Okkels, H.: Bull. d'histol. appliq. à la physiol. **6**:321, 1929.

Reimann and Fritsch,[4] in a number of investigations on human subjects, found that when the number of red blood corpuscles is below 4,000,000 per cubic millimeter, the rise in their number is about seven times as large when ferrous salts are administered as when ferric salts

TABLE 1.—*Observations on Patient 1**

Date	Hemoglobin, per Cent	Erythrocytes	Reticulocytes, pro Mille	Treatment
1/23	38	5,405,000	12	Ferric hydroxide, 5 cg.
1/26	39	.....	12	
1/29	42	.....	8	
2/ 2	43	6,010,000	21	
2/ 5	..	.....	12	
2/ 9	42	6,030,000	11	Ferrous salt, 5 cg.
2/12	49	.....	6	
2/16	47	.....	7	Ferrous salt, 10 cg.
2/19	48	.....	..	
2/23	62	.....	2	
2/26	76	.....	15	
3/ 1	78	.....	6	
3/ 4	82	6,600,000	1	
3/ 7	75	.....	0	
3/10	78	.....	1	
3/14	82	5,850,000	3	
3/18	81	.....	0	

* Aged 11 months (five weeks premature); twin brother of patient 2; affected with rickets, emotional convulsions and anemia. Free hydrochloric acid was present in the gastric juice.

TABLE 2.—*Observations on Patient 2**

Date	Hemoglobin, per Cent	Erythrocytes	Reticulocytes, pro Mille	Treatment
1/23	35	4,145,000	8	Ferrous salt, 5 cg.
1/26	37	.....	13	
1/29	43	.....	54	
2/ 2	50	5,280,000	16	
2/ 5	..	.....	28	
2/ 9	64	5,915,000	15	Ferric hydroxide, 5 cg.
2/12	63	.....	3	
2/16	62	.....	3	
2/19	58	.....	..	
2/23	63	.....	0	
2/26	65	.....	1	
3/ 1	72	.....	1	Ferrous salt, 10 cg.
3/ 4	75	6,115,000	15	
3/ 7	66	.....	10	
3/10	68	.....	13	
3/14	73	6,385,000	8	
3/18	80	.....	2	

* Aged 11 months (five weeks premature); same condition as that of patient 1.

are given, even though the amount of the ferric salt is far greater than that of the ferrous salt. It makes no difference whether ferrous chloride or ferrous sulphate is used.

4. Reimann, F., and Fritsch, F.: Ztschr. f. klin. Med. **115**:13, 1930; **117**:304, 1931.

The clinical effect of ferric salts is due to their being partly reduced in the intestinal tract.

Reduced iron is dissolved as ferrous chloride if there is free hydrochloric acid in the stomach, and 10 cg. of reduced iron is dissolved in 35 cc. of tenth-normal hydrochloric acid—an amount which is present in the stomach under normal conditions (Reimann and Fritsch)—forming a ferrous compound, which may be absorbed.

Iron may, however, also be dissolved in the small intestine, the contents of which have an acid reaction (p_H 4.5 to 6.5). The amount of iron converted also depends on the dose administered, and in small doses, reduced iron is inefficacious in cases of achylic anemia, a fact which supports this diagnosis against that of chlorosis (Faber). Mettier

TABLE 3.—*Observations on Patient 3* *

Date	Hemoglobin, per Cent	Erythrocytes	Reticulocytes, pro Mille	Treatment
3/13	42	4,650,000	20	Reduced iron, 10 cg.
3/18	44	.....	15	
3/21	50	4,565,000	7	
3/24	44	4,110,000	15	
3/25	..	.....	..	Ferrous salt, 10 cg.
3/28	54	4,990,000	36	
3/31	52	5,230,000	30	
4/ 4	61	5,180,000	22	Ferric hydroxide, 10 cg.
4/ 9	60	4,700,000	3	
4/12	60	4,860,000	6	
4/16	59	4,570,000	15	Ferrous salt, 10 cg.
4/19	59	5,140,000	15	
4/23	64	5,555,000	21	
4/26	65	6,120,000	23	
4/30	68	6,005,000	19	

* Aged 10 months (four weeks premature); suffered from rickets and anemia; had intercurrent suppurative otitis on April 4 to 11. Free hydrochloric acid was obtained.

and Minot [5] have drawn a chart which shows that ferrous salts are effective in spite of achylia, while ferric citrate is effective only when the acidity of the stomach contents is great.

The effect of the small amounts of iron in iron-containing mineral waters is due to its being present mostly as ferrous carbonate.

Previously copper was not considered necessary to the human organism. In a series of works, Elvehjem and his collaborators [6] proved the necessity of copper in rats, and especially the effect of copper on nutritional anemia.[7] Myers and Beard [8] showed that manganese, arsenic

5. Mettier, S. R., and Minot, G. R.: Am. J. M. Sc. **181**:25, 1931.

6. Elvehjem, C. A., and Kemmerer, A. R.: J. Biol. Chem. **93**:189, 1931. Elvehjem, C. A.: Relative Value of Inorganic and Organic Iron in Hemoglobin Formation, J. A. M. A. **98**:1047 (March 26) 1932.

7. Elvehjem found organic iron and ferric chloride inefficacious. He has not tried a ferrous compound.

8. Myers, V. C., and Beard, H. H.: J. Biol. Chem. **94**:71, 1931.

and several other substances have an effect similar to that of copper. If copper is necessary for the human organism, infants may suffer from the lack of it, cow's milk containing only one-third the amount in human milk (from 0.02 to 0.06 mg. per hundred cubic centimeters [Zondek [9]]). The amount of copper in the liver is greatly reduced

TABLE 4.—*Observations on Patient 4**

Date	Hemoglobin, per Cent	Erythrocytes	Reticulocytes, pro Mille	Treatment
3/18	26	3,210,000	4	Ferric hydroxide, 5 cg.
3/21	26	3,415,000	26	
3/24	26	3,550,000	17	
3/28	26	3,850,000	24	Reduced iron, 5 cg.
3/31	30	4,045,000	22	
4/ 4	37	4,510,000	18	
4/ 9	42	4,945,000	36	Ferrous salt, 5 cg.
4/12	42	4,470,000	20	
4/16	44	.....	25	
4/19	49	5,095,000	23	
4/23	51	4,650,000	40	Ferrous salt, 10 cg.
4/26	55	4,590,000	53	
4/30	72	4,650,000	35	
5/ 3	69	.....	..	
5/ 9	75	.....	..	

* Aged 22 months (four weeks premature); suffered from rickets and anemia; had a fever during most of the treatment, especially on March 22 to 25 and April 10 to 16. Free hydrochloric acid was obtained.

TABLE 5.—*Observations on Patient 5**

Date	Hemoglobin, per Cent	Erythrocytes	Reticulocytes, pro Mille	Treatment
3/24	66	4,835,000	15	Ferric hydroxide, 5 cg.
3/28	62	5,210,000	9	
3/31	61	4,940,000	8	
4/ 4	58	4,885,000	13	Reduced iron, 5 cg.
4/ 9	61	5,540,000	18	
4/12	61	5,615,000	8	
4/16	65	5,100,000	8	Ferrous salt, 5 cg.
4/19	72	5,470,000	17	
4/23	71	5,800,000	7	
4/26	75	5,980,000	8	
4/30	75	5,815,000	6	

* Aged 10 months; suffered from rickets and anemia; had pyuria with a slight elevation of temperature from March 18 to April 12.

during the first months of life (from 3 mg. to from 0.3 to 1.5 mg. per hundred cubic centimeters). The amount of copper in cow's milk may be doubled by pasteurization in copper vessels. French authors (Gorter [10] and others) have not found any lack of copper in children

9. Zondek, S. G., and Bandman, M.: Klin. Wchnschr. **10**:1528, 1931.

10. Gorter, E.; Grendel, F., and Weyers, W. A. M.: Rev. franç. de pediat. **7**:747, 1931.

with anemia. Schiff [11] did not obtain any definite effect in treating the anemia of children with copper compounds, while Lewis,[12] who treated thirty-four children with ferrous carbonate and certain others with cupric sulphate, secured a marked effect with the copper compound.

Most cases of anemia in children, however, are due to a scarcity or iron in the food, to infections, to too early birth or to twin birth (Lichtenstein).

The effect of copper compounds is not clear, and the effect of ferrous salts as compared with ferric salts is not much known outside the German countries; also, to my knowledge, their effect on anemia in children has not previously been investigated.

PRESENT INVESTIGATIONS

The aim of my investigations has been to examine the effect of ferrous and ferric compounds, reduced iron and a copper compound on anemia in children.

TABLE 6.—*Observations on Patient 6* *

Date	Hemoglobin, per Cent	Erythrocytes	Reticulocytes, pro Mille	Treatment
3/24	42	5,380,000	19	Ferric hydroxide, 5 cg.
3/29	43	5,375,000	13	
3/31	38	5,210,000	22	
4/ 4	41	5,290,000	17	Reduced iron, 5 cg.
4/ 9	42	5,380,000	18	
4/12	42	5,120,000	6	Ferrous salt, 2 doses
4/16	51	4,830,000	22	
4/19	56	5,210,000	23	
4/23	52	5,270,000	12	

* Aged 12 months (six weeks premature); suffered from anemia; had otitis with elevation of temperature on April 8 to 14; transferred to another hospital on April 25, owing to suspicion of whooping cough.

The preparations used were ferrous chloride (or ferrous sulphate), dissolved in a simple syrup, and colloidal ferric hydroxide. They were made and controlled by the chemist of Rigshospitalet, Dr. Schou, and each contained 5 cg. of iron in 5 cc. Ferrous salts are easily oxidized, and become ferric salts. It is therefore necessary to add a little citric acid and keep them exposed to light. The reduced iron used was the purest product obtainable.

The tables show the treatment given and the results of the hematologic examinations. None of the patients reacted to the tuberculin test. Patients 1 and 2 were enzygotic twins.

11. Schiff, E.: Klin. Wchnschr. **9**:2144, 1930.

12. Lewis, M. S.: Iron and Copper in the Treatment of Anemia in Children, J. A. M. A. **96**:1135 (April 4) 1931.

The effect of the two iron compounds on anemia was very different. The ferrous salt quickly caused a rise in the hemoglobin percentage, the ferric hydroxide having but slight effect.

After some time, when the effect was definite, the ferrous and ferric compounds were interchanged, and the hemoglobin percentage at once rose in the child who now received ferrous salt, while the one who now received the ferric compound did not show further improvement. During one period the dose of the iron compound was doubled, half of the preparation being lost through vomiting.

Patients 3, 4 and 5 were first treated with ferric hydroxide, then with reduced iron and lastly with ferrous chloride. In none of these

TABLE 7.—*Observations on Patient 7* *

Date	Hemoglobin, per Cent	Erythrocytes	Reticulocytes, pro Mille	Treatment
3/ 4	65	5,755,000	2	Ferric hydroxide, 5 cg.; cupric sulphate, 0.5 mg.
3/ 7	69	.....	11	
3/10	65	.....	8	Ferric hydroxide, 5 cg.; cupric sulphate, 2 mg.
3/14	71	5,690,000	14	
3/18	68	6,200,000	5	Ferric hydroxide, 5 cg.; cupric sulphate, 10 mg. (abundant vomiting)
3/20	..	.....	..	Ferric hydroxide, 5 cg.; cupric sulphate, 2 mg.
3/21	68	6,390,000	2	Reduced iron, 5 cg.; cupric sulphate, 1 mg.
3/25	67	5,835,000	8	
3/28	65	6,520,000	0	
3/31	65	6,180,000	2	Ferrous salt, 5 cg.; cupric sulphate, 1 mg.
4/ 4	77	6,140,000	17	
4/ 9	78	6,390,000	30	
4/12	80	6,420,000	12	
4/19	75	6,190,000	13	

* Aged 10 months (three weeks premature); twin brother of patient 8; suffered from rickets and anemia. Free hydrochloric acid was found.

cases was an effect of the ferric hydroxide on the hemoglobin percentage seen; in two of three cases there was some effect from reduced iron, while the ferrous salt was effective every time it was given. Patient 5, suspected of having whooping cough, was removed to another hospital before the ferrous salt was given. In one of the cases 5 cg. during twenty-four hours had only a slight effect, the hemoglobin percentage increasing considerably when the dose was doubled. The reaction of the reticulocytes and the red blood corpuscles was less characteristic.

Patient 6 first received reduced iron, then a ferrous salt and lastly ferric hydroxide to make sure that the hydroxide was not effective only when administered after the other two substances. When the administration of the ferrous salt was discontinued, the rise ceased at once, but reappeared when the ferrous salt was again administered.

Examination showed in every case the superior effect of ferrous salt on anemia in children.

On another pair of enzygotic twins (cases 7 and 8) the effect of adding cupric sulphate to the three iron preparations used was tried, one of the twins receiving the cupric sulphate. The same ideal conditions for control were present as in the first pair of twins. The ferric hydroxide, with or without the addition of cupric sulphate, was without effect; in one case reduced iron had a moderate effect, while in both patients the ferrous salt caused a considerable rise in the hemoglobin

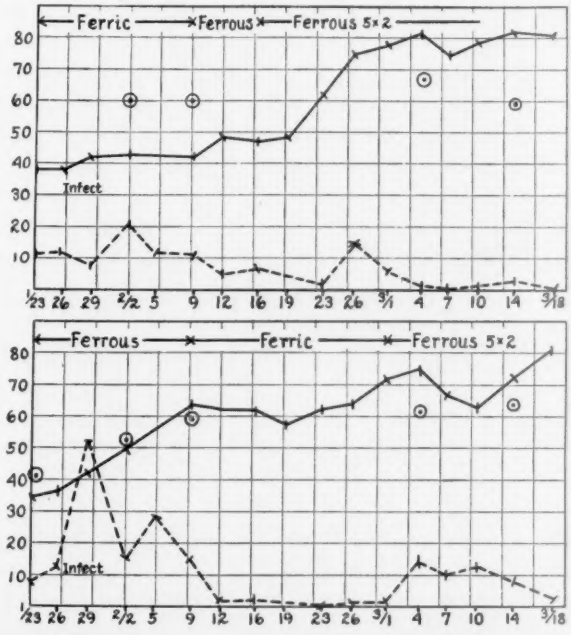

Chart illustrating the effect of the administration of ferrous salts and ferric hydroxide. The solid line indicates the percentage of hemoglobin; the dotted line, the number of reticulocytes pro mille; the dot and circle, the number of erythrocytes, expressed in hundred thousands.

percentage. The cupric sulphate seemed to be without effect on the hemoglobin. As may be seen from the tables, the amount of cupric sulphate administered differed (the amount must not be too large, or the cupric sulphate will act as an emetic).

Thus, ferrous salts are the most effective iron compounds for the treatment of simple anemia, but they also possess other advantages. Of fourteen persons (doctors, nurses and medical students) who were given 25 cg. of reduced iron (a small therapeutic dose), seven had heart-burn, two who suffered from dyspepsia felt quite ill, with

aggravation of their dyspeptic symptoms, and all except one had evil smelling and tasting eructations of hydrocarbons and hydrogendisulphide, originating in impurities in the iron. The same persons took 27 cg. of ferrous sulphate (i. e., 10 cg. of iron, the ordinary therapeutic dose) several times without discomfort. Only one person had tasteless eructations.

Thus, there is no doubt that for the treatment of simple anemia ferrous compounds should be used (ferrous sulphate, chloride, lactate or carbonate).

TABLE 8.—*Observations on Patient* 8 *

Date	Hemoglobin, per Cent	Erythrocytes	Reticulocytes, pro Mille	Treatment
3/ 4	51	4,910,000	4	Ferric hydroxide, 5 cg.
3/ 7	54	.....	9	
3/10	47	.....	16	
3/14	55	4,850,000	13	
3/18	55	5,400,000	4	
3/21	56	5,520,000	2	Reduced iron, 5 cg.
3/25	55	5,305,000	28	
3/28	57	5,615,000	17	
3/31	61	5,810,000	7	Ferrous salt, 5 cg.
4/ 4	65	6,110,000	10	
4/ 9	72	5,935,000	17	
4/12	76	.....	36	
4/19	81	5,380,000	12	

* Aged 10 months (three weeks premature); same condition as that of twin (patient 7).

SUMMARY

The effect of ferrous and ferric ions and reduced iron on anemia in children was investigated.

Ferrous salts cause a quick and considerable rise in the hemoglobin percentage, while ferric preparations seem to be without effect.

Reduced iron is effective in certain cases.

The addition of cupric sulphate seems to be without effect.

Unlike reduced iron, ferrous preparations do not cause dyspeptic symptoms.

Ferrous preparations are preferable for the treatment of simple anemia.

BLOOD LIPIDS IN CHILDREN WITH SCARLET FEVER AND RHEUMATIC DISEASE

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Determinations of blood lipids in man and in animals have frequently been made, and several reports have recently been published on studies of the cholesterol content of the blood of children in health and in disease. Most of the determinations have been made on the blood of infants under 2 years of age. The determination of lipids reported in the present study were made on the blood plasma of normal children of various ages and on that of children with scarlet fever and with rheumatic disease. The investigation was undertaken to see if the values for blood lipids in children with scarlet fever and with rheumatic disease differed from those obtained in similar studies on normal children.

It is a well established fact that the cholesterol content shows marked variations in certain diseases, notably, in diabetes and nephrosis. It has also been assumed that other pathologic conditions may influence the amount of cholesterol in the blood plasma. Bloor [1a] has shown that the content not only of cholesterol but also of other blood lipids is altered in certain acute infections. Certain queries naturally arise: Are these changes due to inadequate or altered diet? Are the plasma lipids influenced by the presence of some toxic substance? Are the deviations from normal the same in any disease, or do certain specific infections bring about changes which are peculiar to those diseases?

Determinations of total lipids, phospholipids, cholesterol and residual fat were made on the blood plasma of twenty-nine healthy or so-called normal children, of forty-three children who were in the acute or convalescent stage of scarlet fever and of forty-two who showed acute or chronic manifestations of rheumatism. Similar determinations were made on the blood plasma of twenty-one children suffering from diseases other than scarlet fever or rheumatism. The methods employed were those described by Bloor[1b] for the determination of small amounts

This study was aided by a grant from the Rockefeller Research Foundation.

From the Department of Pediatrics, the University of Rochester School of Medicine and Dentistry, and Strong Memorial Hospital.

Much assistance was given in this study by Dr. W. R. Bloor, Dr. S. W. Clausen and Miss Augusta McCoord.

1. Bloor, W. R.: J. Biol. Chem. (*a*) **77**:53, 1928; (*b*) **82**:273, 1929; (*c*) **25**: 577, 1916.

of lipids in the blood plasma. Specimens of blood taken while the subjects were in a fasting state were collected in citrate tubes (15 cc.) and in most cases were brought directly to the laboratory. Samples of the blood were placed in the centrifuge for from one quarter of an hour to three hours after collection. Immediately after centrifugation the ratio of corpuscles to plasma was determined and the plasma was run into an alcohol-ether extract, 5 cc. of plasma being used to 100 cc. of the extract.

The total fatty acids and cholesterol were determined together in a portion of alcohol-ether extract of plasma by saponification, extraction of the acidified residue with petroleum ether and oxidation of an aliquot of the solution with a sulphuric acid-dichromate reagent. The cholesterol was determined calorimetrically in another aliquot. The phospholipids were determined by the oxidative method of Bloor. Fifteen cubic centimeter portions of alcohol-ether extract were used for the combined determinations of total lipids and cholesterol, and 10 cc. aliquots of petroleum-ether extract for separate determinations. Fifty cubic centimeter portions of alcohol-ether extract were used for determinations of the phospholipids. The determinations of the total lipids and of the cholesterol were made in duplicate on different days. Since there was sufficient alcohol-ether extract for only one determination of the phospholipids for each sample of blood, the method was checked by frequent determinations on a sample of known phospholipid content.

Studies on the lipid content of the blood of twenty-nine normal children were recorded. These children were living temporarily in an institution and were apparently free from disease. They had been living a fairly normal life, though they were confined somewhat more closely than if they had been living in their own homes. The diet was the usual institutional diet. The amount of protein, fat and carbohydrates actually consumed was calculated. There was considerable variation in the amount of food taken, but the average for the twenty-nine children was 130 Gm. of protein, 90 Gm. of fat and 550 Gm. of carbohydrates. There were only four girls among the twenty-nine subjects. All the children, with the exception of two boys, were 8 years of age or more. Only four determinations were made in May; the remainder were made during the winter months.

The individual determinations for the twenty-nine normal children as well as the average for the group are recorded in table 1. It is evident that the average phospholipid and cholesterol content of the blood plasma is considerably lower than that in adults. The normal cholesterol values were recorded by Bloor[1c] as 220 mg., by Wade[2] as 165 mg. and by Hunt[3] as 177 mg. per hundred cubic centimeters. The available data on the blood lipids in children are usually restricted to the determinations of cholesterol and phospholipids. The average cholesterol value (150 mg.) in the twenty-nine normal children studied may be compared with the findings of Gordon and Cohn,[4] who gave the average for cord blood as 89 mg. per hundred cubic centimeters and that for children up to 2 years of age as from 110 to 190 mg. Manicatide, Bratesco and Rusesco,[5] using Grigaut's method on serum, gave an average of 131 mg. for subjects under 4 months of age, and an average of 116 mg. for those from 4 months to 1 year of age. For all

2. Wade, P. A.: Am. J. M. Sc. **177**:790, 1929.

3. Hunt, H. M.: New England J. Med. **201**:659, 1929.

4. Gordon, M. B., and Cohn, D. J.: Cholesterol and Lipoid Phosphorus in Infancy and in Childhood; Normal Incidence in Cord Blood and During Infancy and Early Childhood, Am. J. Dis. Child. **35**:193 (Aug.) 1928.

5. Manicatide, M.; Bratesco, A., and Rusesco, A.: Compt. rend. Soc. de biol. **96**:1240, 1927.

babies, whether artificially fed or breast-fed, they took as their average 125 mg. Baylac and Sendrail,[6] using Grigaut's method on serum gave 149 mg. as the average, and Varone's[7] results were rather lower, 115 mg. being given as the normal amount of cholesterol for infants under 1 year of age, and 137 mg. as the average for children from 2 to 8 years of age. Boyd,[8] using Bloor's method, gave

TABLE 1.—*Lipid Content of the Blood Serum of Normal Children* *

Case	Month	Sex	Age	Mg. per 100 Cc. of Plasma				Ratio of Cholesterol to Phospholipids
				Total Lipids	Phospholipids	Cholesterol	Residual Fat	
1	May	M	5	305	86	147	27	1.71
2	March	M	7	409	92	168	96	1.83
3	January	M	8	422	123	138	133	1.12
4	March	M	8	367	73	121	137	1.66
5	December	M	9	514	107	166	194	1.55
6	December	F	9	554	118	201	174	1.70
7	December	M	10	468	102	151	174	1.48
8	December	F	10	469	112	149	171	1.33
9	December	F	10	532	96	189	185	1.97
10	December	M	11	428	90	144	152	1.60
11	December	M	11	513	95	172	192	1.81
12	December	M	11	377	98	123	127	1.25
13	March	M	11	367	78	120	135	1.54
14	January	M	12	361	79	125	121	1.58
15	December	M	13	444	109	153	145	1.40
16	December	M	13	468	103	150	174	1.46
17	January	M	13	478	107	158	170	1.48
18	January	M	13	551	118	176	208	1.49
19	January	M	13	450	126	122	183	0.97
20	January	M	13	316	58	108	115	1.86
21	March	M	13	423	87	167	115	1.92
22	January	M	14	423	139	136	126	0.98
23	May	M	14	403	82	181	77	2.21
24	January	M	15	419	95	136	154	1.43
25	January	M	15	382	84	153	97	1.82
26	May	M	15	332	67	130	92	1.94
27	May	M	15	327	69	134	80	1.94
28	December	F	15	522	105	183	178	1.74
29	January	M	16	357	81	135	101	1.67
			Average for Group					
Maximum				554	139	201	208	
Minimum				305	58	108	108	
Average				427	90	150	139	
Adult average				600	220	220	110	
Standard deviation, average					±18 (20%)	±22 (14%)		

* A balanced diet averaging 3,665 calories, with 130 Gm. of protein, 90 Gm. of fat, and 550 Gm. of carbohydrates, was given.

6. Baylac, J., and Sendrail, M.: Bull. et mém. Soc. méd. d. hôp. de Paris **52**:33, 1928.

7. Varone, L.: Riv. di clin. pediat. **27**:599, 1929.

8. Boyd, G. L.: Blood Cholesterol in Diabetic Children, Am. J. Dis. Child. **38**:490 (Aug.) 1929.

185 mg. as the average for children. Ward,[9] using the method described by Leiboff,[10] examined fifty-nine normal children from an orphanage between the ages of 6 and 13. The results showed that a consistent level of blood cholesterol is maintained throughout childhood. In boys, this level shows a steady and progressive rise up to the age of puberty. In girls, the amount of variation at every age was found to be markedly greater than that shown by boys. The cholesterol level in girls tended on the average to be somewhat lower than that in boys at every age. As there were only four girls in our group of twenty-nine normal children, no comparisons can be made between the values for the two sexes; in the few determinations made, the lipid content for the girls was slightly higher than that for the boys of like ages. No reliable deductions could be made as to the difference in the levels of blood lipids within the group, as the majority of the subjects were over 10 years of age. The relatively few determinations made showed no significant difference between the cholesterol level in children 8 years of age and that in children 12 years of age.

No fair comparison can be made between lipid values determined in cold weather and those determined in warm weather, as only four determinations were made in May. However, comparing the average of the readings taken in May with the average of the twenty-five readings taken in winter, one notes a slight difference:

	Total Lipids	Phospho-lipids	Choles-terol	Residual Fat
Average of 4 determinations in May (mg.).....	342	76	148	69
Average of 25 determinations in cold months (mg.)....	468	99	150	151

The values for cholesterol were found to be practically unchanged during the warmer months, but those for the phospholipids, total lipids and residual fat were considerably lower.

No definite relationship can be found between the amount of fat ingested and the lipid values. Children consuming smaller amounts of fat showed values as high as those of children taking nearly twice as much fat. This was also true with reference to the intake of protein and of carbohydrates. The highest phospholipid reading was in a boy, aged 14, who consumed the greatest number of calories (5,142). With this exception the lipid values showed the same variations, whether 3,000 or 4,000 calories was taken.

Similar determinations of lipids were made on the blood plasma of forty-three children with scarlet fever. The same method of collecting and examining the blood was employed as with the normal children. In only two of the forty-three children was the blood taken after the third week of illness. At the time of the withdrawal of the blood the majority of the children were afebrile and had passed the acute stage of the disease. One or more complications existed at the time of the withdrawal of the blood in about half of the children. Though the scarlet fever patients were on the regular hospital diet, it was found that they ingested on the average considerably more fat and less protein than did the normal children. As recorded in table 2, the total number of calories consumed by each group was about the same. A more equal distribution of the two sexes was noted in the patients with scarlet fever: there were nineteen girls and twenty-four boys. The number of boys and girls under 10 years of age was the same, fourteen in each

9. Ward, K. M.: Arch. Dis. Childhood **6**:329 (Dec.) 1931.

10. Leiboff, S. L.: J. Biol. Chem. **61**:177, 1924.

TABLE 2.—*Lipid Content of the Blood Serum of Children with Scarlet Fever* *

Case	Month	Sex	Age	Mg. per 100 Cc. of Plasma: Total Lipids	Phospholipids	Cholesterol	Residual Fat	Ratio of Cholesterol to Phospholipids	Complications and Course
1	January	M	3	514	108	167	192	1.54	Chorea
2	May	F	4	596	106	215	202	2.03	Treated with serum
3	May	F	5	676	164	274	156	1.69	Treated with serum
4	May	F	5	479	73	156	196	2.13	Cervical adenitis
5	February	F	6	564	107	207	182	1.93	Otitis; chronic diabetes
6	May	F	6	473	112	191	112	1.70	
7	May	F	6	597	102	224	193	2.19	Treated with serum; cervical adenitis
8	May	M	6	340	68	120	115	1.79	Otitis media
9	May	F	6	428	73	159	141	2.18	
10	May	M	6	475	96	181	140	1.88	
11	May	F	7	306	76	127	65	1.67	Otitis media
12	May	F	7	257	58	93	79	1.61	Erythema multiforme
13	May	M	7	496	92	204	129	2.21	Otitis media
14	May	F	7	442	93	163	136	1.75	Otitis media; cervical adenitis
15	May	M	7	482	93	204	114	2.18	Cervical adenitis, 52d day
16	May	F	7	421	74	149	148	2.01	
17	May	M	8	473	100	128	214	1.28	Erysipelas, 106th day
18	May	M	8	503	77	158	215	2.05	Otitis media; mastoidectomy
19	May	M	8	423	79	135	168	1.70	Treated with serum; cervical adenitis
20	May	M	8	467	85	185	133	2.17	Endocarditis
21	May	F	9	477	79	180	153	2.26	
22	February	M	9	469	100	183	128	1.83	Acute arthritis
23	May	F	9	480	108	201	107	1.83	Sinusitis
24	May	M	9	365	102	144	81	1.41	
25	May	M	9	616	96	230	207	2.39	
26	May	F	9	304	58	92	127	1.69	
27	January	M	10	580	76	192	241	2.52	Chorea
28	June	M	10	500	116	137	217	1.18	
29	December	M	11	594	117	256	132	2.18	
30	January	M	11	482	96	190	133	1.90	
31	May	M	11	446	75	152	163	2.02	
32	February	F	11	274	61	111	67	1.81	Cervical adenitis
33	May	F	11	430	85	155	141	1.82	
34	February	M	12	416	117	151	112	1.29	Chronic diabetes
35	May	M	12	508	95	209	131	2.20	Acute rheumatic fever
36	June	F	12	342	83	118	110	1.42	
37	December	M	13	349	72	119	123	1.65	
38	June	F	13	478	80	147	204	1.83	
39	June	F	13	437	95	105	216	1.10	
40	February	M	13	357	75	139	99	1.85	
41	December	M	14	395	82	161	99	1.96	
42	May	M	15	356	55	132	121	2.40	
43	February	F	7	523	97	218	131	2.24	Chronic endocarditis
				Average for Group					
Maximum				676	164	270	241		
Minimum				257	55	92	65		
Average				451	90	167	143		
Standard deviation, average					±20 (22%)	±42 (25%)			

* The regular hospital diet, averaging 3,888 calories, with 94 Gm. of protein, 175 Gm. of fat and 550 Gm. of carbohydrates, was given. The blood was taken within four weeks of the onset except in two cases, in which it was taken on the fifty-second day and on the one hundred and sixth day.

group. The average age of patients with scarlet fever was less than the average age of the normal children. More determinations were made in the summer months than during cold weather.

	Total Lipids	Phospho-lipids	Choles-terol	Residual Fat
Average of 31 determinations in May and June (mg.)..	446	88	163	146
Average of 12 determinations from December to February (mg.)	459	92	173	136

Comparison of determinations made in summer and those made in winter showed little difference, though the averages for total lipids, phospholipids and cholesterol were slightly lower in the determinations made in summer, as was also the case in the normal children.

Comparison of the average determinations for boys and those for girls showed that they were almost identical in the children with scarlet fever:

	Total Lipids	Phospho-lipids	Choles-terol	Residual Fat
Average for 19 girls (mg.)	447	89	164	140
Average for 24 boys (mg.)	454	89	168	146

Contrasting the results obtained in the forty-three patients with scarlet fever with those obtained in the twenty-nine normal children, it was found that the values for phospholipids were the same, while those for total lipids, for cholesterol and for residual fat were slightly higher in the patients with scarlet fever. This condition existed in spite of the fact that in the group with scarlet fever more determinations were made in warm weather, when the values were shown to be slightly lower than in cold weather. The average intake of fat was nearly twice as great in the patients with scarlet fever as in the normal children.

Similar determinations of lipids were made on the blood plasma of forty-two children with rheumatic disease. Twenty-two of these children were in the acute stage of the disease at the time of the withdrawal of the blood, and twenty were in the chronic stage. They have been grouped separately in tables 3 and 4. All the children listed as having acute rheumatism had the clinical manifestations of rheumatic fever, and more than half of them had rheumatic endocarditis as a complication. The group was equally divided between boys and girls. The average age of the children with acute rheumatic fever was 8½ years, while that of the children with chronic rheumatic disease was 11 years. The intake of food of the children with acute rheumatic fever was less than that of the children who had scarlet fever. The average intake was 68 Gm. of protein, 97 Gm. of fat and 206 Gm. of carbohydrates. An equal number of determinations on the blood plasma of children with acute rheumatic disease was made in the winter and in the summer months.

	Total Lipids	Phospho-lipids	Choles-terol	Residual Fat
Average for 11 determinations from May to July (mg.)	419	79	141	171
Average for 11 determinations from December to April (mg.)	509	104	163	159

As in the case of the normal children and those with scarlet fever, the lipid levels of the children with acute rheumatic disease, with the exception of that of residual fat, were lower in the warmer months. The average value of the plasma lipids of these children was similar to that found in normal children. There was, however, a greater variation in the phospholipid and cholesterol levels in acute rheumatic disease. Similar results were obtained by Ward in eleven determinations made on children with acute rheumatic disease.

TABLE 3.—*Lipid Content of the Blood Serum of Children with Acute Rheumatic Disease* *

Case	Month	Sex	Age	Mg. per 100 Cc. of Plasma: Total Lipids	Phospholipids	Cholesterol	Residual Fat	Ratio of Cholesterol to Phospholipids	Clinical Manifestations
1	March	M	4	596	109	177	257	1.62	Mild rheumatic fever; recovered
2	March	F	4	453	87	149	78	1.71	Severe rheumatic fever, endocarditis; died
3	December	F	5	354	84	126	109	1.49	Moderate rheumatic fever; recovered
4	December	M	5	503	125	206	111	1.64	Moderate rheumatic fever; recovered
5	May	F	5	499	122	179	149	1.47	Severe rheumatic fever, endocarditis; died
6	November	F	5	491	141	150	172	1.07	Severe rheumatic fever, endocarditis, pneumonia; died
7	May	M	7	537	129	185	173	1.43	Moderate rheumatic fever; recovered
8	May	F	7	488	150	168	136	1.12	Moderate rheumatic fever; recovered
9	May	F	7	424	65	127	190	1.95	Moderate rheumatic fever, endocarditis; recovered
10	June	F	7	532	99	127	257	1.29	Moderate rheumatic fever; recovered
11	May	F	7	257	58	93	79	1.60	Moderate rheumatic fever, erythema multiforme; recovered
12	January	F	8	450	98	165	137	1.68	Severe rheumatic fever, endocarditis; recovered
13	[June 11]	M	9	[301	21	72	179]		
	{June 18}			{399	25	129	188}	2.39	Severe rheumatic fever; recovered
	[July 5]			[550	109	165	229]		
14	April	M	9	373	61	146	113	2.39	Severe rheumatic fever, endocarditis; recovered
15	February	M	9	469	100	183	128	1.83	Moderate rheumatic fever; recovered
16	December	M	10	372	57	151	108	2.65	Moderate rheumatic fever; recovered
17	April	M	11	374	83	138	112	1.66	Severe rheumatic fever, endocarditis; recovered
18	June	F	11	450	66	144	190	2.18	Moderate rheumatic fever; recovered
19	July	F	11	373	16	126	173	7.87	Moderate rheumatic fever, chronic endocarditis; recovered
20	May	M	12	508	95	209	131	2.30	Mild rheumatic fever; recovered
21	June	M	14	444	46	120	233	2.61	Moderate rheumatic fever; recovered
22	April	M	14	311	61	110	105	1.80	Moderate rheumatic fever, endocarditis; recovered
				Average for Group					
Maximum				596	150	209	257		
Minimum				257	16	72	78		
Average				464	91	152	165		
Standard deviation, average					±34 (37%)	±46 (30%)			

* The regular hospital diet, averaging 2,027 calories, with 68 Gm. of protein, 97 Gm. of fat and 206 Gm. of carbohydrates, was given.

TABLE 4.—*Lipid Content of the Blood Serum of Children with Chronic Rheumatism* *

Case	Month	Sex	Age	Mg. per 100 Cc. of Plasma				Ratio of Cholesterol to Phospholipids	Clinical Manifestations
				Total Lipids	Phospholipids	Cholesterol	Residual Fat		
1	January	M	3	514	108	167	192	1.54	Chorea, following scarlet fever
2	March	F	5	351	63	98	162	1.55	Chronic rheumatic fever, recurrent
3	March	M	6	846	177	370	178	2.09	Chronic rheumatic fever, recurrent
4	February	F	7	523	97	218	131	2.24	Chronic rheumatic fever, endocarditis
5	May	F	8	561	156	183	180	1.17	Chorea, chronic rheumatic fever, endocarditis
6	June	F	8	416	83	129	167	1.55	Chronic rheumatic fever, pneumonia, endocarditis
7	May	F	9	480	108	201	107	1.86	Chronic rheumatic fever, sinusitis
8	January	M	10	580	76	192	241	2.52	Chorea, following scarlet fever
9	March	M	10	416	117	185	61	1.58	Chronic rheumatic fever
10	April	M	10	450	96	126	197	1.48	Chronic rheumatic fever, endocarditis
	June			547	114	185	193		
11	July	M	11	543	156	146	220	0.93	Chorea, following acute rheumatic fever
12	March	M	11	367	78	120	135	1.54	Growing pains, severe, 2 years
13	April	M	12	431	100	124	178	1.24	Chronic rheumatic fever
14	December	M	12	416	83	129	167	1.55	Chronic rheumatic fever
15	May	F	12	345	140	101	100	0.72	Chronic rheumatic fever, acute tonsillitis
16	June	M	12	466	60	123	241	2.05	Chronic rheumatic fever, acute endocarditis
17	Dec. 30	M	13	400	71	138	131	1.31	Chronic rheumatic fever, endocarditis, nodules
	Feb./32		14	441	131	128	146		
18	December	F	13	418	77	156	133	2.02	Chronic rheumatic fever, endocarditis
19	June	M	14	468	88	216	85	2.45	Chronic rheumatic fever
20	March	F	14	505	101	158	201	1.56	Chronic rheumatic fever
				Average for Group					
Maximum				846	177	370	241		
Minimum				345	60	98	61		
Average				476	104	163	164		
Standard deviation, average					±33 (31%)	±58 (35%)			

* The regular hospital diet, averaging 2,497 calories, with 97 Gm. of protein, 100 Gm. of fat and 286 Gm. of carbohydrates, was given.

Among the twenty children with chronic rheumatic disease a greater variety of clinical manifestations was noted. Chorea was present in four, while more than half of the children had endocarditis associated with chronic rheumatism. The average age of these children was nearly three years more than that of the children with acute rheumatism. The intake of food of the children with chronic rheumatism was slightly more than of those with acute rheumatism. All the rheumatic children, those with the acute as well as those with the chronic form of the disease,

TABLE 5.—*Lipid Content of the Blood Serum of Children with Various Diseases* *

				Mg. per 100 Cc. of Plasma				Ratio of Cholesterol to Phospholipids	
Case	Month	Sex	Age	Total Lipids	Phospholipids	Cholesterol	Residual Fat		Clinical Disease
1	May	M	2	1,209	376	403	352	1.13	Nephrosis
2	June	M	2	1,194	281	360	467	1.29	Nephrosis
3	February	F	3	2,860	550	625	1,555	1.13	Nephrosis
4	March	F	3	549	152	241	86	1.58	Convulsions (epilepsy ?)
5	March	F	3	307	100	92	101	0.92	Erythroblastic anemia
6	July	M	3	563	110	180	220	1.63	Erythroblastic anemia
7	January	F	5	350	146	87	122	0.59	von Jaksch's anemia
8	May	M	5	470	100	141	192	1.41	Lymphatic leukemia; died
9	February	M	6	226	72	77	63	1.07	Infectious arthritis
10	January	M	6	458	97	157	158	1.62	Acute osteomyelitis
11	February	M	6	428	100	172	103	1.72	von Jaksch's anemia
12	January	M	6	587	103	200	218	1.94	Nephritis, acute
13	January	F	7	458	155	167	104	1.08	Nephritis, acute
14	January	M	7	610	101	167	292	1.65	Meningococcic meningitis
15	August	M	7	790	219	163	400	0.74	Nephritis, acute; died
16	May	F	8	370	92	143	94	1.55	Hypertension
17	January	F	8	560	150	258	73	1.72	Tuberculous peritonitis
18	January	F	9	425	60	109	222	1.81	Septicemia; died
19	January	F	10	335	57	115	125	2.01	Dermatomyositis
20	January	F	10	533	141	148	217	1.05	Nephritis, acute
21	October	F	11	1,171	257	320	520	1.25	Nephritis, subacute; died
				Average for Group					
Maximum				2,860	550	625	1,555		
Minimum				226	57	77	63		
Average					162	225			
Standard deviation, average					110 (67%)	127 (56%)			

* A varied diet depending on the nature of the disease averaging 2,018 calories with 62 Gm. of protein, 98 Gm. of fat and 207 Gm. of carbohydrates, was given.

were hospital patients and were confined to their beds at the time the blood was examined. More determinations were made in the winter months than in the summer months. The average seasonal differences were as follows:

	Total Lipids	Phospholipids	Cholesterol	Residual Fat
Average for 8 determinations from May to July (mg.)	478	113	160	161
Average of 12 determinations from November to April (mg.)	479	100	168	161

There was less difference in the average values in summer and in winter than existed in similar determinations made in normal children and in those with scarlet fever and acute rheumatism. The phospholipid and cholesterol values are some-

what higher for the children with chronic rheumatism than for those with acute rheumatism and with scarlet fever. The value for cholesterol corresponds with that of the twenty-three determinations of cholesterol recorded by Ward, who offered an explanation for this condition, stating that in acute juvenile rheumatism the average percentage of cholesterol in the blood is normal but that in chronic rheumatism it shows a definite tendency to be greater than normal. It is suggested tentatively that this abnormally high level of cholesterol is related to the disordered growth which frequently attends chronic juvenile rheumatism.

Additional studies were made on twenty-one children under 12 years of age who had a variety of clinical conditions other than scarlet fever and rheumatism. A number of these children were extremely ill, which may account for the variations in the lipid levels. Extreme variations were noted in the children with nephrosis. In other diseases the variations were not much greater than those found in scarlet fever and in rheumatism.

TABLE 6.—*Average Comparative Values of the Plasma Lipids in Normal and in Sick Children*

Condition	Number of Cases	Average Age	Average Intake of Fat, Gm.	Average Calories	Average Fat, per Cent	Mg. per 100 Cc.				Standard Deviation	
						Total Lipids	Phospholipids	Cholesterol	Residual Fat	Phospholipids	Cholesterol
Normal	29	12	90	3,665	22	427	90	150	139	±18	±22
Scarlet fever	43	9	175	3,888	40	451	90	167	143	±20	±42
Acute rheumatic fever	22	8	97	2,027	43	464	91	152	165	±34	±46
Chronic rheumatic fever	20	11	100	2,497	37	476	104	163	164	±33	±58
Nephrosis and nephritis	8	6	91	1,549	33	1,100	260	298	478	135	152
Other diseases	13	6	137	2,207	55	434	103	150	143	±66	±62

COMMENT

The plasma lipids in children are subject to considerable fluctuation in health and in disease. However, a fairly constant level is maintained in healthy children. In our determinations the maximum and minimum values for healthy children showed less deviation from the mean than was noted in groups of children with some disease. The formula for calculating the standard deviation, $\mu = \sqrt{\Sigma \frac{(d^2)}{n}}$, in which $\Sigma\ (d^2)$ represents the summation of the squares of the individual deviations from the mean and n the number of determinations, was used, and the standard deviation was then expressed in units and percentage. Table 6 brings out the fact that the phospholipid and cholesterol levels are only slightly higher in children with scarlet fever and in those with rheumatism than in normal children, but the standard deviation expressed in units is considerably greater in disease, especially as pertains to cholesterol. Whether these marked deviations are due to a greater variation in diet, especially in the amount of fat ingested, or to the presence of an infection is not certain. Among the normal children no constant relationship could be found between high lipid

levels and a high intake of fat or of carbohydrates. Though maximum lipid values are likely to be recorded in healthy children who consume 4,000 calories or more a day, similar maximum values were noted in children taking between 2,000 and 3,000 calories a day. Within the range of the diet usually consumed by healthy children over 8 years of age the values for lipids show no definite relationship to lesser or greater amounts of fat and carbohydrate in the diet. This conforms with the observations of Boyd that diets high in fat did not cause hypercholesteremia, nor did lowering the intake of fat reduce a previously high content of cholesterol in the blood plasma.

Determinations of the blood lipids in four children in a metabolism ward, who received a measured amount of a proprietary milk powder,

TABLE 7.—*Lipid Content of the Blood Serum of Four Children with Chorea Whose Diets Were Carefully Controlled* *

Patient	Month	Sex	Age	Day of Diet	Total Calories	Protein, per Cent	Fat, per Cent	Carbohydrate, per Cent	Mg. per 100 Cc. Total Lipids	Phospholipids	Cholesterol	Residual Fat
T. A.	July	M	9	3	1,884	24	35	41	631	...	148	...
				13	1,884	24	35	41	730	116	183	381
				17	1,884	24	35	41	754	314	190	260
M. C.	May	F	9	2	1,731	23	35	42	533	112	191	171
				12	1,731	23	35	42	578	94	196	221
E. D.	July	M	7	7	1,731	23	35	42	542	156	145	220
				17	1,731	23	35	42	799	173	179	420
J. S.	August	F	8	11	1,884	24	35	41	569	118	229	146
				18	1,884	24	35	41	888	181	323	282

* The diets consisted of a measured amount of a proprietary milk powder, eggs, lactose, cream and orange juice.

eggs, lactose, cream and orange juice, show that when the fat in the diet is derived from certain sources, such as eggs and cream, the lipid content of the blood can be increased above normal. This is more noticeable after the children have been on this special diet for ten days. Table 7 shows how a controlled diet will usually cause an increase in the phospholipids and cholesterol. Such an increase is generally not noted in a normal child on the usual diet.

It would seem, therefore, that the deviations in the plasma lipids are influenced by factors other than the amount of fat ingested. In her study of ninety diabetic children Boyd concluded that there is a tendency toward hypercholesteremia in severe malnutrition and also in hydremia. A condition of severe malnutrition existed in a few of the children with chronic rheumatic disease, and marked hydremia was present in the children with nephrosis and in some of those with

nephritis, but high phospholipid and cholesterol values were also noted in children who showed no evidence of malnutrition or hydremia. It is quite likely that the presence of an infection was responsible for the greater deviation in the children with scarlet fever and rheumatism. In those instances in which several determinations were made on children who were acutely ill, the deviations from the mean were greatest at the onset of the infection and approached normal variations after the infection had subsided. In general, the more severe the infection the greater was the deviation from the mean.

The seasonal variations noted in the lipid levels are suggestive though not conclusive. Determinations made in the summer or warm months

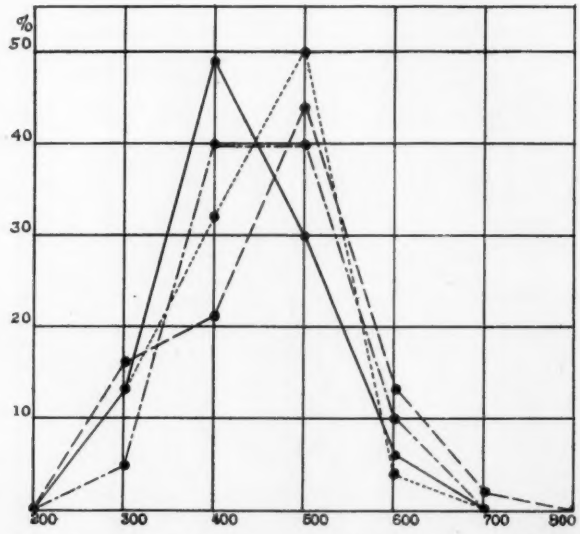

Chart 1.—Distribution of values for total lipids in normal children and in those with scarlet fever and with acute and chronic rheumatic fever. In this and the accompanying charts the solid line indicates the normal group; the dash line, the children with scarlet fever; the dotted line, those with acute rheumatism, and the dot and dash line, those with chronic rheumatism.

were uniformly lower on the average than those made in the winter or cold months. This applies to the determinations made on healthy and on sick children. It is probable that these differences can be explained by the effect of changes in temperature on fat metabolism or on the amount of activity.

In the attempt to discover the effect of such infections as scarlet fever and rheumatism on the lipid values the total range of variation of these values in normal and in sick children was divided into four or five equal intervals, and the number of cases falling into each interval was determined. The percentage of cases in each interval

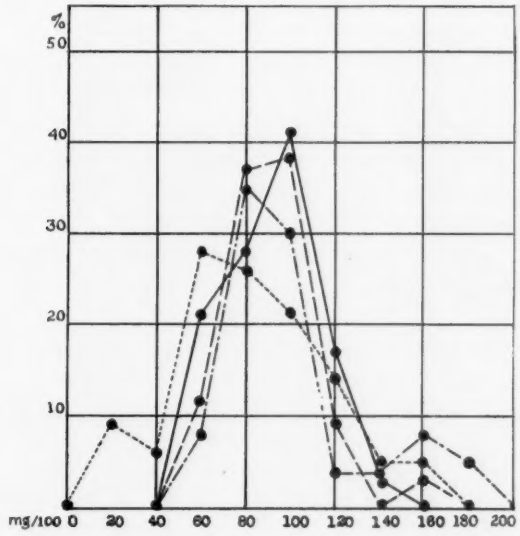

Chart 2.—Curve of phospholipid values in normal children and in those with scarlet fever and with acute and chronic rheumatic fever.

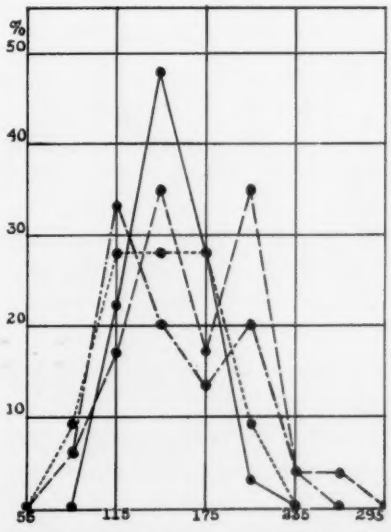

Chart 3.—Curve of cholesterol values in normal children and in those with scarlet fever and with acute and chronic rheumatic fever.

was calculated, and these figures were plotted as ordinates above the midpoint of the corresponding interval as abscissa. The points were connected by straight lines. The curves may thus be readily compared. The peak of each curve indicates the interval in which most cases fall. Any deviations of the pathologic groups from the normal group are readily apparent. Such deviations include displacement of the peaks, spreading of the curves and asymmetry caused by the presence of a relatively large number of high or low values. The mean and the probable error of the mean were also calculated where a sufficient difference seemed to exist.

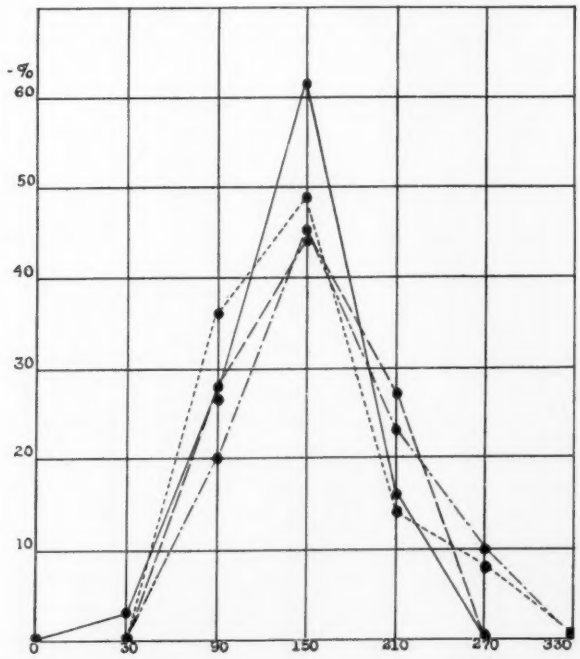

Chart 4.—Curve of values for residual fat in normal children and in those with scarlet fever and with acute and chronic rheumatic fever.

A study of chart 1 shows that the values for total lipids in children with chronic rheumatism are distributed in the same manner as the normal values. In scarlet fever and in acute rheumatic fever higher values occur, but the differences are probably not of statistical significance. There is also more variation in scarlet fever. In both acute rheumatism and scarlet fever the curve of distribution is asymmetrical, owing to the presence of high values.

Chart 2 shows that the phospholipid curve in normal children is regular. The distribution of phospholipid values for children with

scarlet fever closely resembles that for normal children. Some of the values for phospholipids in the cases of chronic rheumatism are distinctly high. In acute rheumatic fever there is a wide range of values, with a distinct tendency toward low values.

A study of chart 3 shows a fairly uniform distribution of cholesterol values in normal children. The distribution in acute rheumatic fever is similar to that in health. The distribution in chronic rheumatic fever and scarlet fever, however, shows a tendency toward two peaks, but the number of cases is too small to establish this beyond a doubt. If true, it would mean that in each condition a significant number of subjects showed high values.

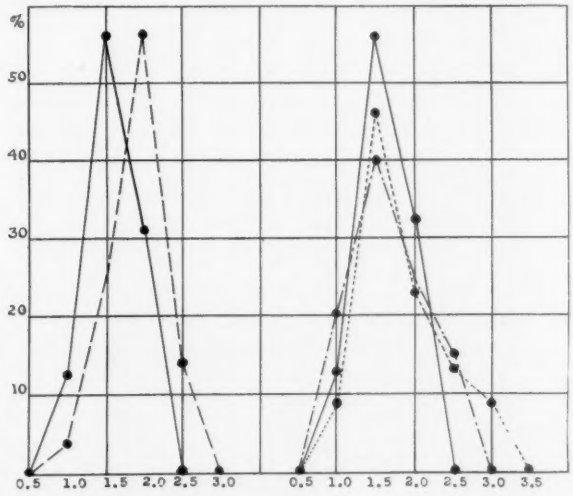

Chart 5.—Curve of values for the $\frac{\text{cholesterol}}{\text{phospholipids}}$ ratio in normal children and in those with scarlet fever and with acute and chronic rheumatic fever.

Chart 4 shows that the values for residual fat have a similar distribution in normal and in sick children.

The data for chart 5 were obtained by utilizing the ratios of cholesterol to the phospholipids for the individual cases as noted on the first four tables. These ratios were reduced to percentages, and the ratio percentage for each group was plotted. It is noted that the ratio $\frac{\text{cholesterol}}{\text{phospholipids}}$ seems to be slightly higher than normal in scarlet fever and in certain cases of acute rheumatic disease. In scarlet fever the difference is statistically significant and may be due to either the diet or the infection. In both acute and chronic rheumatic fever there is a distinct tendency for high values to occur, but in view of the small number of cases, it is not possible to claim that this difference is not due to chance.

SUMMARY

Values for blood lipids in twenty-nine normal children between the ages of 5 and 16 were fairly constant, but were considerably below the accepted averages for normal adults.

Values for blood lipids in forty-three children convalescing from scarlet fever were practically the same as in normal children. Deviations from the mean were considerably greater, especially for cholesterol.

Similar values for lipids were found in twenty-two children with acute rheumatism and in twenty with chronic rheumatism. The standard deviations were much greater for the children with rheumatism than for the normal children.

Values for blood lipids deviated considerably from the normal in nephrosis and in nephritis.

Values for blood lipids were not influenced by ordinary variations in diet. The deviations from the mean noted in normal and in sick children seemed to bear no relationship to an increased or diminished intake of fat and of carbohydrates.

No appreciable difference was noted between determinations made on boys and those made on girls. Similar deviations were found in both sexes.

Determinations made in the summer months were uniformly lower than determinations in the winter months.

Studies on the blood lipids of children with rheumatic disease and with scarlet fever revealed values similar to those found in normal children. The standard deviation from the mean was considerably greater in the children with these infections than in the normal children. It is quite likely that the infection rather than the varied amount of fat ingested was responsible for the increased deviations.

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TREATMENT OF OBESITY IN A GROUP OF CHILDREN

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Reduction cures in childhood are considered dangerous by many laymen as well as by some physicians, and unless certain fundamental principles are observed, the procedure is not without an element of danger.

The relative energy requirements of a child are considerably in excess of those in adult life. The total daily caloric requirement of a child has four components: (1) the basal caloric requirement, which constitutes the minimum energy needed to enable the body functions to be carried on properly when at rest; (2) sufficient calories to cover the energy used up in muscular work; (3) additional energy for stimulation of cells by ingested food, and (4) requirements for growth and development of new tissues.

Children's dietaries must provide for all four components of the total daily metabolism. In reduction cures, however, it is of great importance not only to diminish the total caloric intake so that the body has to draw on its own fat reserves, but to see that the growth is not interfered with; therefore, protein and other elements necessary for growth have to be supplied in proper quantity.

Another principle one must not lose sight of is that if the total caloric intake is lowered for a long time the basal metabolic rate becomes lower. At this lower level, the previous diet may no longer lead to loss of weight, because the energy requirement of the body is lowered.

Helmreich [1] observed that the basal metabolic rate increased gradually after the child's diet was increased to a double amount, so that after from two to three weeks the level of the basal metabolic rate increased 20 per cent. Then, after the diet had been diminished to the previous amount, the basal metabolic rate gradually decreased and within fourteen days reached the primary level. Helmreich concluded that there is an equilibrium between the caloric intake and the basal metabolic level. In reducing the weight of obese children, one must aim to keep the basal

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1. Helmreich, E.: Der Grundumsatz im Kindesalter, Ergebn. d. inn. Med. u. Kinderh. **35**:604, 1929; Der Kraftwechsel des Kindes, Berlin, Julius Springer, 1926.

metabolic rate on a normal level in order to create favorable conditions for the normal development of a growing body.

It is well known that feeding a diet high in protein will keep the basal metabolic rate on a high level. Lusk [2] found that when "a large quantity of protein is ingested day after day, then the usual specific dynamic action occurs and also a continued 'secondary' rise in total day-to-day metabolism."

Therefore, in planning a diet for loss of weight, a daily high percentage of protein should be allowed in order that the secondary rise in basal metabolism will offset the reduction of the metabolic plane caused by the lowered total intake.

In this paper we present the results of treatment in twenty-five cases of exogenous obesity in children, twelve boys and thirteen girls, ranging from 5 to 14 years of age. Treatment was carried on over periods of from two to ten months. We recognize the possibility of an endocrine factor in all cases of deviation from normal development in childhood—excessive overweight, overheight and underheight—but the fact remains that in this group of children physical examination and laboratory tests failed to reveal any pathologic changes except an excessive weight. The roentgenograms of the sella turcica showed it to be in every case normal as to both size and contour. A history of overfeeding was obtained in every case. The children were accustomed to diets rich in carbohydrates and relatively high in fats, partaking abundantly of such foods as pastries, candies, starchy foodstuffs, butter, ice-cream, milk and bread. They ingested very little of the bulky low caloric vegetables and fruits. The food was often highly seasoned, and the intake of fluid in the majority of cases was very high. Many of the mothers admitted giving the child from four to six glasses of water daily in addition to from four to eight glasses of milk. Many of the children had a voracious appetite, and took food between meals as well as at the regular mealtimes, the total caloric intake in many cases being twice as much as needed.

Physical examination showed a general distribution of excess fat tissue in all cases. In none was there the pelvic girdle obesity usually associated with pituitary dysfunction. In other words, in this series we were dealing with a group of children in whom we believe obesity was purely nutritional.

Tables 1 and 3 give the essential data obtained on the boys and girls prior to treatment; tables 2 and 4 give the corresponding data obtained after treatment. The basal metabolic rate was measured by the Pirquet [3]

2. Lusk, G.: The Elements of the Science of Nutrition, ed. 4, Philadelphia, W. B. Saunders Company, 1928, p. 278.

3. Pirquet, C.: An Outline of the Pirquet System of Nutrition, Philadelphia, W. B. Saunders Company, 1922; System der Ernährung, Berlin, Julius Springer, 1919.

sitting height standard, which agrees with the Talbot [4] standard, based on height alone. All tests of the basal metabolism were made with the subjects in the postabsorptive state under accepted standard conditions. Every child had an initial practice test several days before the first recorded test, so as to eliminate such factors as excitement or nervousness due to unfamiliarity with the procedure.

TABLE 1.—*Essential Data for Boys Before Treatment*

	Age		Standing Height,	Sitting Height,	Weight		Nutritional State		Basal Metabolism—Heat Production: Total Calories per 24 Hrs.		
Case	Yrs.	Mos.	Cm.	Cm.	Kg.	Lbs.	Pelidisi	Baldwin-Wood % Overweight	Obtained	Predicted	Deviation
1	8	—	130.0	72.0	42.5	93½	104	47	1,128	1,036	+ 8
2	10	—	141.0	78.0	61.8	136	109	76	1,312	1,216	— 7
3	10	—	148.0	77.5	49.7	109½	103	30	1,330	1,185	+12
4	10	—	134.5	70.0	40.8	90	106	28	1,080	980	+10
5	10	2	141.0	77.0	51.1	112½	104	45	1,296	1,185	+ 8
6	10	4	141.5	75.0	41.7	92½	100	20	1,224	1,125	+ 8
7	10	6	150.0	82.0	69.3	152½	108	67	1,250	1,320	— 5
8	11	—	135.0	76.0	53.6	118	107	68	1,156	1,155	± 0
9	12	—	145.0	77.0	60.8	134	111	57	1,406	1,185	+12
10	12	6	150.0	79.0	58.1	128	106	59	1,322	1,248	+ 4
11	12	6	136.0	73.0	40.4	89	106	25	1,180	1,065	+10
12	13	6	165.0	86.0	69.6	153½	103	26	1,608	1,475	+ 8

TABLE 2.—*Essential Data for Boys After Treatment*

	Age		Standing Height,	Sitting Height,	Weight		Nutritional State		Basal Metabolism—Heat Production: Total Calories for 24 Hrs.			Result of Treatment			
													Loss of Weight		
Case	Years	Months	Cm.	Cm.	Kilograms	Pounds	Pelidisi	Baldwin-Wood, % Overweight	Obtained	Predicted	Deviation	Duration of Treatment, Months	Kilograms	Pounds	Increase in Standing Height, Cm.
1	8	10	136.0	75.0	36.3	80	95	14	1,248	1,125	+10	10	6.1	13½	6.0
2	10	7	144.5	79.0	52.5	115½	102	36	1,204	1,248	— 3	7	9.1	20	3.5
3	10	6	150.5	79.0	44.0	97	96	5	1,310	1,248	+ 5	6	5.7	12½	2.5
4	10	2	136.5	71.0	36.3	80	101	12	1,090	1,000	+ 9	2½	4.5	10	2.0
5	10	5	144.0	79.0	45.0	99	97	18	1,250	1,248	± 0	3½	6.1	13½	3.0
6	10	6	144.5	76.5	37.2	82	95	0	1,210	1,155	± 5	2	4.7	10½	3.0
7	11	..	154.0	82.5	60.0	132	102	34	1,392	1,320	+ 4	6	9.3	20½	4.0
8	11	7	144.0	79.0	48.1	106	99	26	1,200	1,248	— 3	7	5.5	12	9.0
9	12	4	148.0	79.0	51.3	113	101	26	1,346	1,248	+ 8	4½	9.5	21	3.0
10	13	1	155.0	81.0	53.1	117	100	15	1,442	1,382	+ 4	7	5.0	11	5.0
11	11	6	138.0	73.0	35.9	79	100	6	1,148	1,065	+ 8	6	4.5	10	2.0
12	14	4	170.0	88.0	64.6	142½	98	5	1,565	1,550	+ 1	10	5.0	11	5.0

The nutritional state was measured by the Baldwin-Wood [5] scale and by the Pirquet pelidisi. Benedict [6] said that "the use of the pelidisi of Pirquet has a great advantage over the ordinary rather gross clinical indications, as an index of the state of nutrition." According to this

4. Talbot, F. B.: Physiol. Rev. **5**:477, 1925.

5. Baldwin, B. T., and Wood, T. D.: Weight-Height Age Tables, Mother & Child **4**:337, 1923.

6. Schattuck, G. C., and Benedict, F. G.: Am. J. Physiol. **96**:524, 1931. Mason, E. D., and Benedict, F. G.: Indian J. M. Research **19**:75, 1931.

standard, the normal range of the pelidisi of children of the ages in our group should be from 95 to 98.

The majority of the children had a large skeleton and were overheight. Table 5 shows the deviation from the average height, as compared with the Baldwin-Wood [5] and the Holt [7] standards. These findings

TABLE 3.—*Essential Data for Girls Before Treatment*

	Age		Standing Height,	Sitting Height,	Weight		Nutritional State		Basal Metabolism—Heat Production: Total Calories per 24 Hrs.		
Case	Yrs.	Mos.	Cm.	Cm.	Kg.	Lbs.	Pelidisi	Baldwin-Wood, % Overweight	Obtained	Predicted	Deviation
13	5	6	108.0	60	26.6	59	104	43	810	720	+10
14	8	2	128.0	69	39.7	87½	107	45	1,008	952	+ 5
15	8	6	125.0	74	41.5	91½	101	60	1,124	1,100	+ 2
16	9	1	128.0	74	41.8	92	101	67	1,280	1,100	+16
17	10	4	138.0	72	45.0	99	106	33	1,152	1,036	+11
18	10	6	145.0	75	65.4	144	116	70	1,275	1,125	+13
19	10	10	133.5	72	49.0	108	110	60	1,155	1,035	+11
20	11	—	154.0	81	63.1	139	106	33	1,382	1,310	+ 5
21	12	—	148.0	80	62.5	137½	107	53	1,250	1,280	— 2
22	12	—	159.0	85	68.1	150	104	31	1,510	1,445	+ 4
23	12	4	160.5	86	76.3	168	106	47	1,591	1,475	+ 7
24	12	6	147.0	80	68.0	149½	111	66	1,400	1,280	+ 9
25	14	2	167.0	84	80.2	176½	111	35	1,632	1,410	+15

TABLE 4.—*Essential Data for Girls After Treatment*

	Age		Standing Height, Cm.	Sitting Height, Cm.	Weight		Nutritional State		Basal Metabolism—Heat Production: Total Calories for 24 Hrs.			Result of Treatment			
													Loss of Weight		
Case	Years	Months			Kilograms	Pounds	Pelidisi	Baldwin-Wood, % Overweight	Obtained	Predicted	Deviation	Duration of Treatment, Months	Kilograms	Pounds	Increase in Standing Height, Cm.
13	6	1	111.5	64.0	22.2	50	95	11	918	820	+11	7	4.0	9	3.5
14	8	6	131.0	72.0	35.2	77½	98	20	1,080	1,036	+ 4	4	4.5	10	3.0
15	8	11	133.0	76.0	37.2	82	95	22	1,152	1,155	± 0	5	4.2	9½	8.0
16	9	6	132.0	75.0	37.0	81½	96	20	1,200	1,125	+ 6	5	4.7	10½	4.0
17	10	8	141.0	75.0	39.2	86½	98	10	1,190	1,125	+ 6	4	5.6	12½	3.0
18	10	10	147.0	76.5	54.6	120	107	33	1,224	1,155	+ 6	4	10.9	24	2.0
19	10	6	137.5	73.5	44.0	97	104	31	1,100	1,075	+ 2	2½	5.0	11	4.0
20	11	2	155.0	82.0	58.6	129	102	22	1,350	1,320	+ 2	2	4.5	10	1.0
21	12	3	150.0	81.0	57.8	127½	102	34	1,340	1,382	— 3	3	4.5	10	2.0
22	12	3	161.5	86.5	62.2	137	99	18	1,513	1,475	+ 2	3	5.9	13	2.5
23	12	6	163.0	88.0	69.5	153	100	30	1,512	1,550	— 2	2½	6.8	15	2.5
24	13	4	150.5	81.0	57.4	126½	103	30	1,384	1,382	± 0	10	10.4	23	3.5
25	14	4	167.5	84.0	72.5	159½	107	22	1,550	1,410	+10	2½	7.7	17	0.5

agree with those of Czerny and Keller.[8] The nutritional state and the size of the frame have a direct relationship to each other. A large, heavy frame requires larger muscles to move it and is also capable of carrying a larger mass of fat and subcutaneous tissue than a smaller one.

7. Holt, L. E.: The Diseases of Infancy and Childhood, ed. 7, New York, D. Appleton and Company, 1916.

8. Czerny, A., and Keller, A.: Des Kindes Ernährung, Ernährungsstörungen und Ernährungs, therapie, ed. 2, Vienna, Franz Deuticke, 1928. Keller, A.: Beobachtungen über Adipositas im Kindesalter, Fortschr. d. Med. **45**:7, 1927.

According to Lucas and Pryor,[9] overweight children are usually the large-boned children, while those with small bones are often underweight.

Mentally, the children in our series were alert, and their intelligence quotients were above the average. However, some had an inferiority complex due to their inability to compete with their schoolmates in athletic activities, and also to the attention attracted by their abnormal weight. In 68 per cent of cases, the basal metabolic rate was a high normal. In 32 per cent, the basal metabolic rate was above normal, probably on a nutritional basis. These results agree with those found for a group of overweight children previously reported.[10]

TREATMENT

Our method was based on the following principles: (1) reduction of the total caloric intake, (2) a high percentage of protein in the diet,

TABLE 5.—*Overheight in Boys and Girls*

	Baldwin-Wood		Holt	
	Boys	Girls	Boys	Girls
10-15 cm.	3	4	3	6
4-10 cm.	4	2	6	1
1- 3 cm.	..	3	..	4
Total	7	9	9	11

(3) limitation of the intake of salt and water and (4) increased muscular activity.

1. By reducing the total caloric intake, the body was compelled to use up its fat reserves in order to cover its dynamic needs. The total caloric intake was based on the determined basal metabolic rate in every case. Bernhardt[11] stated that the patient with exogenous obesity, if held on a diet equal to his own basal metabolic rate, shows a marked loss of weight. The diet given in our series contained 40 per cent protein, 40 per cent carbohydrate and 20 per cent fat. Carbohydrates were given in the form of sugar, a small amount of bread (from 200 to 250 calories) and vegetables and fruits containing 3 and 5 per cent of

9. Lucas, W. P., and Pryor, H. B.: Physical Measurements and Physiologic Processes in Young Children, J. A. M. A. **97**:1127 (Oct. 17) 1931.

10. Topper, Anne, and Mulier, Hannah: Basal Metabolism of Children of Abnormal Body Weight, J. A. M. A. **92**:1903 (June 8) 1929.

11. Bernhardt, H.: Zum Problem der Fettleibigkeit, Ergebn. d. inn. Med. u. Kinderh. **36**:1, 1929; New Concepts Concerning Pathogenesis of Obesity, and Problems of Basal Metabolism, Endocrinology **14**:209, 1930.

carbohydrates. The necessary vitamins were thus adequately supplied, as were also the inorganic salts essential for growth.[12]

In order that the children might develop a taste for foodstuffs of low caloric value (the bulky vegetables), the dishes had to be prepared as appetizingly as possible, and instructions in such preparations were given. (The diet prescribed in every case is presented in table 6.)

2. Protein was given in the form of meat, fish, cheese, eggs and vegetables, and a limited quantity of milk for the younger children. The 40 per cent protein in the basal diet, although relatively high, corresponds to the normal 15 per cent protein of the ordinary diet for the average child.

TABLE 6.—*Daily Intake of Food*

Case	Carbohydrate, Gm.	Protein, Gm.	Fat, Gm.	Total Calories
1	112.5	112.5	23	1,125
2	130	131	26	1,310
3	132	132	26	1,320
4	110	110	22	1,100
5	130	130	26	1,300
6	122	122	24	1,225
7	123	123	25	1,250
8	115	115	23	1,150
9	140	140	28	1,400
10	132	132	26	1,320
11	115	115	23	1,150
12	160	160	32	1,600
13	84	84	16	835
14	100	100	20	1,000
15	112	112	22	1,120
16	128	128	25	1,275
17	115	115	23	1,150
18	127	127	25	1,270
19	115	115	23	1,155
20	138	138	27.5	1,375
21	125	125	25	1,250
22	150	150	30.5	1,510
23	159	159	32	1,595
24	140	140	28	1,405
25	163	163	32	1,635

3. The intake of fluid was restricted to from 500 to 600 cc. (from 15 to 20 ounces) daily, and the total amount of salt did not exceed 5 grains (0.324 Gm.) daily. Many authors, Grafe,[13] Falta,[14] Thannhauser,[15] Bernhardt,[11] Newburgh[16] and others, have stressed the fact that obesity is always associated with retention of water. In fact,

12. Sherman, H. C.: Chemistry of Food and Nutrition, New York, The Macmillan Company, 1928.

13. Grafe, E.: Die pathologische Physiologie des Gesamtstoff- und Kraftwechsels bei der Ernährung des Menschen, Ergebn. d. Physiol. **21**:1, 1923.

14. Falta, W.: Mast- und Entfettungskuren, Wien. klin. Wchnschr. **44**:644 (May 15) 1931; Fettsucht und Inselorgan, ibid. **41**:905 (June 28) 1928.

15. Thannhauser, S. J.: Lehrbuch des Stoffwechsels und der Stoffwechselkrankheiten, Munich, J. F. Bergmann, 1929.

16. Newburgh, L. H.: The Cause of Obesity, J. A. M. A. **97**:1659 (Dec. 5) 1931.

Oertel [17] in planning reduction diets, advocated mainly a limitation of the intake of fluid. Bloch [18] found that a diet limited in salt and fluids tends to decrease the blood chlorides and to eliminate fluids from the body.

4. The influence of muscular activity on the basal metabolism has been recognized since 1898, when Rubner and Heubner [19] observed that a restless infant produced more heat than a quiet one. In fact, not only is there a temporary increase in metabolism due to muscular activity, but, as Benedict and Smith [20] proved, there is a permanent increase in the level of the basal metabolic rate from continued activity. Their figures show that the basal metabolic rate of trained athletes is from 6 to 7 per cent higher than that of nonathletic men. Lauter [21] expressed the belief that lessened muscular activity is the main factor in producing obesity. Bearing this principle in mind, we recommended graduated physical exercise for these obese children. Walking, roller skating, tennis, handball and swimming were among the activities advised.

EFFECTS OF TREATMENT

The effect of the treatment was unquestionably beneficial in every case. The loss of weight was not too rapid, in order that secondary disturbances might be avoided. The figures for the nutritional state at the end of treatment approached normal. The accompanying chart shows two columns, one superimposed on the other, for the pelidisi in every case; the higher column shows the pelidisi at the beginning of the treatment; the shorter, that at the end of treatment. The average duration of treatment was four and one-half months. The total reductions in weight obtained were from 4 Kg. (9 pounds) to 10.9 Kg. (24 pounds); the average loss of weight for the period of treatment was 5.5 Kg. (13⅕ pounds); the average weekly loss of weight was 300 Gm. (¾ pound).

Under our regimen the children continued to grow normally. In fact, in several children an increased growth was noted which was more rapid than the expected normal growth (tables 3 and 4). According to von Pfaundler,[22] accelerated growth in children fed high protein diets may be attributed to stimulation of the thyroid gland by protein.

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17. Oertel, Max Joseph: Allgemeine Therapie der Kreislaufs-Störungen, ed. 4, Leipzig, F. C. W. Vogel, 1891.

18. Bloch, E.: Salzwirkung und Diurese, Ztschr. f. klin. Med. **106**:733, 1927.

19. Rubner, M., and Heubner, O.: Ztschr. f. Biol. **18**:1, 1898; quoted by Talbot.[4]

20. Benedict and Smith: J. Biol. Chem. **20**:243, 1915.

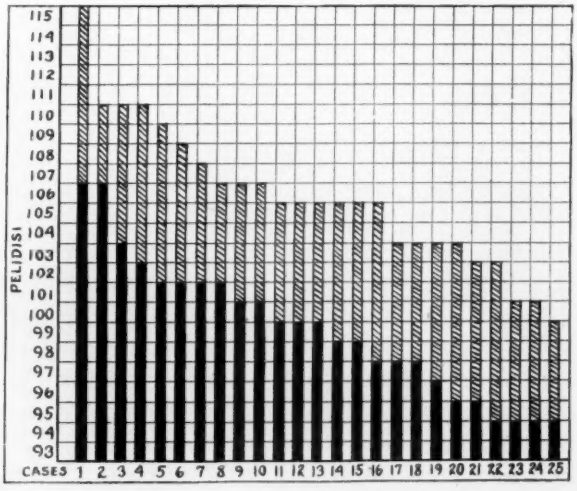
21. Lauter, S.: Zur Genese der Fettsucht, Deutsches Arch. f. klin. Med. **150**:315, 1926; Ueber Beziehungen zwischen Energie und Gewicht bei der Fettsucht, Klin. Wchnschr. **5**:1696, 1926.

22. von Pfaundler, M.: Körpermasstudien an Kindern, Ztschr. f. Kinderh. **14**:1, 1916.

The average increase in standing height was 3.5 cm. (1½ inches). The expected increase in height for the same period should be 2.3 cm. (¾ inch). At the end of treatment the basal metabolism was practically unchanged (tables 3 and 4).

The low caloric diet, which could act as a depressant to the basal metabolism, was evidently offset by the effect of the high percentage of protein in the diet and the increased muscular activity.

We observed also that the children lost their passion for food, so that new habits of feeding were acquired, which persisted after the treatment was finished. A feeling of well-being and an increased capacity for work followed the loss of weight, and an increased interest in studies and school activities was noted.



Two columns, one superimposed on the other, represent the pelidisi in each case. The higher one shows the pelidisi at the beginning of treatment, and the shorter, at the end of treatment. The difference between the pelidisi at the beginning and that at the end of treatment is clearly portrayed.

The problem of overfeeding in children is recognized by Czerny,[8] who gave it an important place in his studies. He held that overfeeding is responsible for a lowered resistance to infectious diseases, resulting in notoriously higher mortality in obese children. The impaired vitality of the obese, he believed, increased also the postoperative mortality. He expressed the opinion that overfeeding leads to such conditions as gastric and intestinal disorders, abnormal retention of water, lymphoid hyperplasia and premature sexual development. He found that overfeeding in children with exudative diathesis often provokes eruptions of the skin and mucous membranes, bronchitis, asthma and other condi-

tions. Joslin [23] has emphasized the correlation of obesity with diabetes. He expressed the belief that "the individual who is overweight is at least twice, and at some ages forty times as liable to diabetes."

When one considers the dangers of obesity, one realizes that prophylaxis against it in childhood is of great importance. It should be the duty of the physician to warn parents of the possible undesirable consequences of overfeeding, and he should control such a tendency.

SUMMARY

This paper presents a study of the treatment of twenty-five children with exogenous obesity. The treatment consisted of measures to insure:

1. A low caloric intake (table 6) to force the body to use up its own stores of fat.

2. A high protein content in the diet to stimulate growth and metabolism.

3. Reduction of salt and water to eliminate retention of water in the body.

4. Increased physical activity to stimulate metabolism.

The treatment resulted in:

1. A loss of weight of from 4 Kg. (9 pounds) to 10.9 Kg. (24 pounds). The average loss of weight was 5.5 Kg. (13⅕ pounds).

2. An average increase of growth of 3.5 cm. (1½ inches). The expected growth for the same period was 2.3 cm. (1 inch).

3. Maintenance of a normal basal metabolism.

4. Better eating habits, with a feeling of well-being, an increased capacity for physical activity and an increased interest in school studies and activities.

23. Joslin, E. P.: The Treatment of Diabetes Mellitus, Philadelphia, Lea & Febiger, 1928.

SO-CALLED THYMIC HYPERPLASIA

IV. A FOLLOW-UP STUDY OF THIRTY CASES

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AND
G. E. ANTHONY, M.D.
DETROIT

The purpose of this paper is to set forth additional evidence for data obtained in an investigation [1] on the pathology of so-called thymic death. In this study it was found that edema of the lungs which cannot be explained on the basis of any cardiac or renal disease, and which is suggestive of an allergic origin, is a constant finding in so-called thymic death. Therefore it seemed to be of interest to examine a number of patients with a previous roentgen diagnosis of thymic hypertrophy for the purpose of discovering any possible association with allergy.

Recent literature on the thymic problem is full of controversies. The questions mainly under discussion concern the following points: What constitutes a normal, and what a large, thymus? [2] Is death produced by obstruction of the trachea? [3] What is the function of the thymus gland? Is one justified in giving roentgen treatment over the gland on obtaining roentgen evidence of its enlargement? Since none of these questions is directly concerned with the present study, no attempt is made to review the literature on this subject or to go into any of these controversies. One problem, however, deserves consideration. Following the painstaking research of Young and Trumbull,[4] there has been a rather general agreement on the fact that status thymicolymphaticus does not exist. Indeed, recent literature indicates that the diagnosis of thymic death has often been the dumping ground for otherwise unexplained deaths.[5] On studying the literature, one

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From the Allergy Clinic, Children's Hospital of Michigan.

1. Waldbott, G. L.: So-Called "Thymic Death": VI. The Pathologic Process in Thirty-Four Cases, Am. J. Dis. Child., this issue, p. 41.

2. Boyd, E.: The Weight of the Thymus Gland in Health and in Disease, Am. J. Dis. Child. **43**:1162 (May) 1932.

3. Marine, D.: Status Lymphaticus, Arch. Path. **5**:661 (April) 1928.

4. Young, M., and Turnbull, H. M.: Analysis of the Data Collected by the Status Lymphaticus Investigation Committee, J. Path. & Bact. **34**:213 (March) 1931.

5. Kennedy, R. L., and New, G. B.: Chronic Stridor in Childhood Sometimes Erroneously Attributed to Enlargement of Thymus, J. A. M. A. **96**:1286 (April 18) 1931.

gains the impression that a rather large number of these cases of so-called thymic death belong in this category. There are, however, a certain limited number of cases in which no pathologic condition, except hyperplasia of the thymus and lymphoid organs, has been demonstrable.

The following considerations prompted this investigation: First, in our work with allergic children, enlargement of lymphoid glands and of the thymus was apparently more frequent than in general pediatric work. The classic lymphoid—eczematous constitution, the facies of the "mouth breather," is encountered in many allergic children. Second,

TABLE 1.—*Manifestations of Exudative Diathesis* *

	Primary	Secondary	Associated with Secondary Manifestations
External skin	Eczema, intertrigo, prurigo	Eczema, impetigo, abscess	Essentially of "nervous nature"; marked itching, restlessness, asomnia, phobias
Mucous membranes	Sudden swellings in various parts of the body	Exudative processes such as tonsillitis pharyngitis	High fever, cough
		Gastro-enteritis,	Refusal to eat, pylorospasm, colic, constipation, muco-membranous colitis
		Coryza, laryngitis, bronchitis, and bronchiolitis; conjunctivitis, blepharitis, balanitis, vulvovaginitis, cystitis	Bronchial asthma, hay fever pseudo-croup, paroxysmal croup
Lymphoid organs	Hyperplasia of adenoids and tonsils. Hyperplasia of palpable lymph glands in neck and joint regions		

* This table is recorded merely as an illustration of the formerly prevalent conception of "thymic" constitution.

in taking histories of allergic patients, it was found in several instances that members of their families, particularly children, had died suddenly, and a diagnosis of thymic death had been made by the physicians in charge. Third, when status thymicolymphaticus was originally described, it was definitely linked with such features as are today considered allergic. A glance at a tabulation of symptoms copied from an early edition of Feer's textbook [6] on pediatrics clearly reveals this fact (table 1).

In our series the diagnosis of thymic hyperplasia has been made on roentgen evidence. The cases were selected from the files of the last six years of the roentgen department of the Children's Hospital of Michigan. While we are not concerned with the question as to whether or not the diagnosis was justified, these cases represent the

6. Feer, E.: Textbook of Pediatrics, Jena, Gustav Fisher, 1919, p. 186.

number in which the diagnosis was made. The fact that only fifty-four cases in which thymic hyperplasia had been diagnosed could be discovered among approximately 16,000 x-ray pictures of the chest indicates that apparently a great deal of conservatism had been employed by those making the diagnosis. In most cases, three films, including a lateral one, had been made before treatment, and only cases in which a distinct misproportion of the thymus gland to the other organs in the chest was found were referred for treatment.

Of the fifty-four patients whose case reports were on file, thirty could be returned to the hospital for reexamination. The following studies were carried out: (1) taking of an allergic history, (2) investigation of the personal history with reference to allergy, (3) skin tests with the most commonly offensive atopens and (4) a check on the former x-ray pictures. Table 2 contains the data obtained.

RESULTS

In this series of thirty cases there were twenty-three male and seven female children, ranging in age from 3 weeks to 5 years. There were eight patients in whom the thymus was extremely large ("size 4") according to x-ray appearance. All the children had presented themselves originally for examination on account of dyspnea. On recent reexamination it was found that twenty-one patients had been suffering from asthma. Eczema was found in eleven. Other symptoms complained of were frequent bronchitis, frequent nasal catarrhs, urticaria, severe headaches, and gastro-intestinal symptoms.

In twenty-six of the thirty cases satisfactory histories could be obtained, which revealed that twenty-one patients came from allergic families. Among the five patients who gave a negative family history of allergy, one (case 18) had eczema and urticaria, two (2 and 5) gave positive reactions to skin tests, and two (23 and 29) were in all probability not allergic. The original complaints of the two latter patients were dyspnea and frequent bronchitis. Of the four patients for whom no satisfactory family history could be obtained, there was one (22) whose condition could be diagnosed as allergy on account of the association of eczema, asthma and marked positive skin reactions. In two others (24 and 25) skin tests were positive. This was corroborated in one (24) by passive transfer tests. In one case (11) there was a history of asthma and headaches and an eosinophilia of 4 per cent. Skin tests were not made in this case.

In summarizing all these data, one can say that in the whole group of thirty patients there were two cases (23 and 29) which showed no evidence of allergy and four (2, 5, 11 and 25) in which such a diagnosis was questionable, while the remaining twenty-four patients appeared to be allergic.

TABLE 2.—*Data Showing Allergic History and Records of Treatment in Thirty Cases Diagnosed as Enlarged Thymus* *

Name	Sex	Date of Treatment	Age at Time of Treatment	Size of Thymus by Roentgenogram	Allergic Symptoms	Family History of Allergy	Effect of Treatment (According to Patients)	Positive Skin Test (Dermal Tests ++ or ++++)	Eosinophilia, per Cent	Comment
R. N.	M	10/30	9 mos.	3	A, N, E, GI	F, E; B, E	None	Not done		
T. S.	M	6/28	5 yrs.	3	Frequent Br and pulmonary infections	Negative	Improved	Feathers, sheep wool, orris root, potatoes	3	Asthma after toxin-antitoxin
A. A.	F	6/30	3 yrs.	2	A, N, E	F, E; M, E	None	Feathers, various epidermals, lamb, cabbage		
N. R.	F	9/28	5 yrs.	4	E	M, hay fever	None	Wool, milk, potatoes	2	
A. M.	M	8/30	1½ yrs.	2	A, N	Negative	None	Oatmeal	5	
E. T.	M	2/31	1¼ yrs.	2	E	F, E; M, E; aunt, E	Improved	Orris root	9	
H. G.	M	3/31	1¼ yrs.	3	N, Br, U	Grandm, A	Improved	Ragweed, orris root	2	
W. A.	M	10/31	1 mo.	2	N, Br	M, A; Grandm, A	Improved	Not done		
B. S.	M	10/28	3½ yrs.	2	N, Br	Uncle, A	Questionable	Egg, milk, ragweed	5	
V. F.	M	4/28	3½ yrs.	2	A, N, E	Grandm, A	Improved	Not done		
P. R.	M	9/28	3 yrs.	4	A, migraine	Unknown	Improved	Not done	4	
C. P.	M	7/28	3 yrs.	4	A	F & B, A	Questionable	Ragweed, foods	6	
W. K.	M	2/30	1 mo.	2	A	F, A	Improved	Not done		
J. R.	M	1/29	4 yrs.	3	A, hay fever	F, hay fever	None	Foods, pollen	1	
N. A.	M	1/26	1 yr.	4	A	F & M, hay fever	None	None	4	Expired during pneumonia
J. K.	M	4/31	2 yrs.	3	A, E	F, hay fever	None	Epidermals, pollen		
R. K.	M	9/28	2 yrs.	3	A, E, vernal catarrh	F, hay fever; B, E	None	Foods, house dust, human hair	5	
B, T.	F	7/32	2 yrs.	4	E, U	Negative	None	Pollen, foods	4	Extreme sensitivity to walnuts
P. G.	M	8/28	6 yrs.	4	A	F & S, hay fever	None	Epidermis, pollen	..	Severe toxin-antitoxin reaction
L. N.	F	7/31	2 wks.	3	A	M, migraine; other members allergic	Improved	Negative		
J. V.	M	Not treated	1 yr.	2	A, seasonal	F, hay fever	.....	Foods, bacteria	4	
N. W.	M	11/31	4 mos.	4	Br, A, E	Unknown	Improved	Egg, wheat, oranges, pollen		
M. M.	M	Not treated	11 mos.	3	A	Negative	.....	Negative	2	
G. W.	F	10/30	1¼ yrs.	4	A, U	Unknown	None	Orange, egg	..	Reagins for orange and egg demonstrated
M. M.	F	6/31	4 mos.	2	A, Br	Unknown	Improved	Foods, pollen	2	
J. O. B.	M	10/29	3½ yrs.	2	E, Br	M, hay fever	Improved	Foods, feathers	2	
M. K.	M	8/32	10 mos.	3	E, A	F, frequent Br	None	Egg, pollen	14	
T. K.	M	10/29	2 yrs.	2	A	B & S, hay fever	None	Foods, pollen, epidermals		
L. L.	F	10/30	3 mos.	2	Frequent Br	Negative	Improved	Negative	1	Passive transfer tests, negative
J. L.	F	8/28	2 mos.	3	A	F, hay fever; M's sister, A	None	Foods, pollen	4	

* A indicates asthma; Br, bronchitis; E, eczema; U, urticaria; N, nasal catarrh; GI, gastro-intestinal symptoms; F, father; M, mother; B, brother; S, sister.

As to the value of the roentgen treatment itself, it is difficult to pass an opinion, because a reduction in the size of the thymus gland observed after several years may indicate only normal involution of the gland. Subjectively, twelve patients of twenty-eight who had received treatment seemed to experience relief from dyspnea. That roentgen therapy does not prevent so-called thymic death was demonstrated to one of us during the study of thirty-four cases that came to autopsy, in two of which roentgen therapy had been given.

COMMENT

The data given indicate that in patients whose condition was diagnosed as status lymphaticus allergic symptoms were of more than incidental occurrence. There are two possible ways of interpreting the data: Either conditions of true allergy are often misdiagnosed as status lymphaticus, or the enlargement of the thymic gland and the lymphoid tissue can be considered as another manifestation of the allergic state. If the latter should be true, it can well be stated that such an enlargement is not a constant manifestation in allergic patients, since, according to our records, routine examination of the chest does not reveal enlargement of the thymus gland in most persons with asthma. This fact, however, does not rule out the possibility that thymic enlargement may be another symptom of the allergic state, if one bears in mind that in only a small group of asthmatic patients are other allergic manifestations, such as eczema and urticaria, encountered simultaneously with asthmatic symptoms.

The problem can therefore be formulated as follows: Is there in certain stages of the allergic constitution, particularly in early life, a tendency toward enlargement of the thymus and other lymphoid organs which may become manifest under certain yet unknown conditions? Is the patient during this stage more susceptible to sudden death? Experimental work to determine these matters is being carried out at present.

During a study by one of us on anaphylactic shock in man [7] the following observations, which may aid in the explanation of this question, were made. Among fifteen cases of sudden death following administration of serum reported in the literature in which autopsy was performed, a definite enlargement of the thymus gland and lymphoid structures was recorded in seven. MacDonald,[8] in a recent study on death due to asthma, showed a definite tendency toward status thymico-

7. Waldbott, G. L.: Human Anaphylactic Shock, J. A. M. A. **98**:446 (Feb. 6) 1932.

8. MacDonald, I. G.: The Local and Constitutional Pathology of Bronchial Asthma, Ann. Int. Med. **6**:253 (Aug.) 1932.

lymphaticus in all his cases, as manifested by the following features: hyperplasia of the lymphoid structures and hypoplasia of the suprarenals and of the vascular organs, especially of the heart and aorta.

In the recent studies of one of us [1] on thirty-four autopsies of sudden unexplained death (collected from the pathology departments of various hospitals), all of which showed the aforementioned features, an additional constant observation could be made: The appearance of the lungs showed a remarkable resemblance to that of the lungs in anaphylactic death, particularly with reference to the vascular structures. Furthermore, there was evidence of asphyxiation in most cases, although no obstruction of the air passages could be found. This asphyxiation was explained on the basis of edema of the lungs which was present. In none of these cases was there a full explanation of the mechanism of death.

It has been previously brought out that any substance, such as pollen, serum, drug or other allergen, may account for death in allergic patients, provided three conditions are fulfilled: (1) a marked sensitivity to the respective agent, (2) rapid absorption of the antigen and (3) a larger dose of the antigen than the patient can tolerate. Regardless of whether or not the antigen instrumental in causing death contains protein, anaphylactic death may occur under the conditions named.

A case of asthma due to the local application of cocaine,[9] another due to ether,[10] and a case of severe vasomotor rhinitis due to ether, have been described recently. Several of the "thymic" deaths were attributed to sensitization to such substances, although this could not be definitely proved.

Baagøe [11] reported a death following the injection of a very small amount of egg extract; Starck [12] reported one following the eating of peas. In the course of our study the following experience was encountered, which may further contribute to the question of the identity of anaphylactic and "thymic" death as the result of extreme sensitivity to food.

B. T. (case 18), 2 years old, showed rather marked reactions to certain foods, ragweed, etc. When skin tests were made by the scratch method for reactions to walnuts, there was noted, immediately on

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9. Waldbott, G. L.: Asthma Due to a Local Anesthetic, J. A. M. A. **99**:1942 (Dec. 3) 1932.

10. Waldbott, G. L.: So-Called Thymic Death: V. Respiratory Sensitization to Local and General Anesthetics, Arch. Otolaryng. **17**:549 (April) 1933.

11. Baagøe, K. H.: Allergic Death After Intracutaneous Injection of Hen Albumen, Ugesk. f. læger **90**:550 (June 14) 1928.

12. von Starck: Primary Specific Allergy and Idiosyncrasic Shock, Monatschr. f. Kinderh. **32**:119, 1926.

application of the powdered material, the appearance of a large wheal, which spread within one minute over the whole back, and within three minutes gave rise to generalized urticaria associated with wheezing. One half cubic centimeter of epinephrine controlled this reaction. The child had been breast fed, and the mother assured us that the patient had never had occasion to come in contact with food containing walnut.

In view of this marked generalized anaphylactic reaction following the application of a small amount of walnut on the skin, it appears rather likely from our experience with other antigens that the child would have died of anaphylactic shock had she partaken of walnut by mouth, considering particularly the marked permeability of the gastrointestinal tract in young children. It is also likely that the patient who had a severe attack of asthma following a local application of cocaine on the nasal mucous membrane would share the same fate if accidentally given an intravenous injection of cocaine for the purpose of local anesthesia.

SUMMARY

1. In thirty children whose condition had been diagnosed by the roentgen method as "enlarged thymus," a follow-up study revealed that twenty-four were afflicted with an allergic disease as evidenced by the history and by skin tests. In four of the remaining cases such a diagnosis was questionable.

2. In one of these cases such marked sensitivity was encountered that a scratch test with walnut produced a definite anaphylactic reaction, although the child had never eaten walnut.

3. The possible relationship of thymic enlargement to anaphylactic death is discussed. Thorough allergic studies in cases with x-ray evidence of enlarged thymus are suggested.

SO-CALLED "THYMIC DEATH"

VI. THE PATHOLOGIC PROCESS IN THIRTY-FOUR CASES

GEORGE L. WALDBOTT, M.D.
DETROIT

Most recent contributors to the literature on so-called "thymic death" are at a loss to explain this phenomenon. Painstaking research during recent years has led to only a few positive observations. The work of the English Status Lymphaticus Investigation Committee [1] on over 600 autopsies tends to question the existence of a thymic diathesis. The diagnosis of thymic death is frequently made the dumping ground of unexplained sudden death (Kennedy and New [2]). Enlargement of the thymus is often diagnosed erroneously on insufficient roentgenographic evidence (Hasley and Di Tomasi [3]). Boyd [4] observed that a large thymus is rather the rule than the exception in patients dying suddenly. The formerly prevalent conception that pressure on the thymus is responsible for so-called "thymic" asthma, and even for death, has lost considerable ground within recent years.

In spite of these various observations tending to deny the original conception of Paltauf that a large thymus is instrumental in causing sudden death, the fact remains that there are patients with hyperplastic lymphoid tissue who die suddenly, and observations made at autopsy give no clue whatsoever to the cause of death. Various reasons have

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The following pathologists cooperated with me in this study: Dr. C. V. Weller, University Hospital, Ann Arbor (8 cases); Dr. A. M. Young and Dr. B. S. Kline, Mount Sinai Hospital, Cleveland (7 cases); Dr. W. H. Chase, McGill University, Montreal (5 cases); Dr. L. J. Rhea, Montreal General Hospital (3 cases); Dr. P. F. Morse, Harper Hospital, Detroit (3 cases); Dr. A. C. Edwards, Children's Hospital, Detroit (2 cases); Dr. B. Steinberg, Toledo Hospital (2 cases); Dr. M. A. Southwick, University of Chicago (2 cases); Dr. W. H. Brosius, St. Joseph's Mercy Hospital, Detroit (1 case); Dr. J. A. Kasper, Herman Kiefer Hospital, Detroit (1 case).

1. Young, M., and Turnbull, H. M.: An Analysis of the Data Collected by the Status Lymphaticus Investigation Committee, J. Path. & Bact. **28**:403, 1930.

2. Kennedy, R. L., and New, G. B.: Chronic Stridor in Childhood Sometimes Erroneously Attributed to Enlargement of Thymus, J.A.M.A. **96**:1286 (April 18) 1931.

3. Hasley, C., and Di Tomasi, R. G.: Cin-ex Camera Studies on the Thymus in Infants and Children, J. Michigan M. Soc. **29**:25 (Jan.) 1930.

4. Boyd, E.: The Weight of the Thymus Gland in Health and Disease, Am. J. Dis. Child. **43**:1162 (May) 1932.

suggested to me a close relationship of the allergic state with what has been called the thymicolymphatic constitution, and have brought up the question of whether or not the mechanism of death in these cases may not be quite similar to, if not identical with, that of human anaphylactic shock as it is observed following injections of serum, pollen and other antigens.

The reasons for this conception are the following:

(1) Thymus in anaphylactic shock. Among fifteen cases of anaphylactic shock following serum injections reported in the literature, enlargement of lymphoid structures were reported in eight (Waldbott [5]).

(2) Thymus in asthma. In a recent report by MacDonald [6] of eight deaths due to asthma, enlargement of the thymus and lymphoid structures was recorded in all cases. Others (Huber and Koessler [7]) have noted similar changes in death due to asthma, although they have not emphasized these lesions in their reports.

(3) Thymus in sudden death following administration of drugs. Of twenty cases of sudden death following administration of local anesthesia, in which autopsies have been reported by various pathologists, hyperplasia of the thymus was present in eleven (Mayer [8]). Jaffé [9] reported that of twenty-six cases of sudden death during general anesthesia in ten cases there was hyperplasia of the thymus and other lymphoid organs. For the last three years I have been looking for instances of sensitization to cocaine, procaine and ether among my allergic patients. I have recently been able to report five such cases of respiratory sensitization.[10]

(4) Thymus in allergic children. In a number of my allergic patients, whose asthma began immediately after birth, the diagnosis of "thymic asthma" had been made by their physicians, because of roentgen evidence of enlarged thymus. While it is difficult to make such a diagnosis on the basis of a single roentgen examination,[3]

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5. Waldbott, G. L.: Prevention of Anaphylactic Shock, with a Study of Nine Fatal Cases, J. A. M. A. **98**:446 (Feb. 6) 1932.

6. MacDonald, I. G.: The Local and Constitutional Pathology of Bronchial Asthma, Ann. Int. Med. **6**:253, 1932.

7. Huber, H. L., and Koessler, K. K.: The Pathology of Asthma, Arch. Int. Med. **30**:685 (Dec.) 1932.

8. Mayer, E.: The Toxic Effects Following the Use of Local Anesthetics, J. A. M. A. **82**:876 (March 15) 1924.

9. Jaffé, R. H., in von Schjerning, O.: Handbuch der ärztlichen Erfahrungen im Weltkriege, Leipzig, Johann Ambrosius Barth, 1921, vol. 8, p. 41.

10. Waldbott, G. L.: So-Called Thymic Death: V. Respiratory Sensitization to General and Local Anesthetics, Arch. Otolaryng. **17**:549 (April) 1933.

Tumpeer [11] concluded, as the result of a thorough follow-up of thirty-eight children, combined with repeated fluoroscopic examinations, that there exists a relationship between infantile allergy and hyperplasia of the thymus and the other lymphoid organs.

(5) Sudden death in allergic families. I have records of members of several asthmatic families who have died suddenly from minor causes, similarly to the way in which patients die from thymic death. For example: a 6 year old son of a patient (G. T.) with hay fever died during a tonsillectomy, soon after the induction of general anesthesia. The 3 year old child of an asthmatic patient (J. A.) died suddenly during a minor infection of the upper respiratory tract. The new-born baby of a patient (L. S.) with hay fever had asthma-like symptoms which lasted for several weeks, and then died suddenly. Autopsy revealed enlargement of the thymus and lymphoid structures. An asthmatic adult (C. H.) died during a minor nasal operation, without apparent cause.

(6) "Thymic" and allergic constitutions. In studying the characteristic features of what has formerly been termed the thymicolymphatic constitution, it is difficult to make a distinction from the manifestation of the allergic make-up. In fact, such symptoms as chronic catarrh of the upper respiratory tract, gastro-intestinal upsets, eczema and eosinophilia, which have been associated with the thymicolymphatic constitution by former clinicians (Waldbott and Anthony [12]), are now definitely regarded as allergic.

While none of these facts is in any way conclusive, they were nevertheless sufficient to stimulate investigation into the possible association of status thymicolymphaticus with status asthmaticus, and the relationship of thymic death to anaphylactic death.

In determining satisfactory methods either to prove or to disprove this relationship, one encounters great difficulties. The diagnosis of status lymphaticus usually cannot be definitely established before death, and after death clinical and immunologic investigation is impossible. When one attempts to study the reported pathologic process present in thymic death and to make comparisons with the pathologic changes seen in anaphylaxis, one again encounters difficulties because the literature records very few thoroughly described cases of death due to anaphylaxis. I, therefore, decided to accumulate as much data as possible on the clinical, pathologic and immunologic factors underlying human anaphylactic shock. The following discussion is an attempt to apply this experience to a study of "thymic death."

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11. Tumpeer, I. H.: Personal communication.

12. Waldbott, G. L., and Anthony, G.: So-Called Thymic Hyperplasia: IV. A Follow-Up Study of Thirty Cases, this issue, p. 34.

Although there are certain reasons for a distinction between anaphylactic and allergic shock in men, many are inclined to consider both types of shock as identical. For reasons outlined elsewhere [13] the differentiation between anaphylactic and allergic shock, if justified at all, is of little importance to the clinician and is, therefore, not applied to this study.

ANAPHYLACTIC SHOCK IN MAN

Probably the most characteristic symptoms of anaphylactic shock occur when an overdose of pollen extract is given (Waldbott [14]). Its mechanism is dependent on three factors: (1) the degree of individual sensitivity, (2) a dose above the patient's tolerance and (3) the rate of absorption. Factors contributing to the effect of an overdose are incomplete absorption of an injection previously given, absorption of additional pollen through the nose as encountered during the pollen season and absorption through the gastro-intestinal tract of substances other than pollen to which the patient is sensitive. An overdose may, therefore, be brought about not only by one antigen absorbed in one manner, but by a multiplicity of causative agents injected, inhaled or absorbed through the gastro-intestinal tract. During the course of these studies on shock following injections of pollen it was observed that the severity of the reaction and its resemblance to the conditions in the experiment with the anaphylactic animal were proportionate to the size of the overdose, the rate of absorption and the patient's degree of sensitivity. When the absorption was slowed down and the overdose was not considerably in excess of the patient's tolerance, any or all known allergic manifestations appeared during the course of the shock.

In a subsequent analysis of eight cases of death due to anaphylaxis following injections of horse serum,[5] the records of which were placed at my disposal, it was found that there was essentially no difference in the mechanism and the symptomatology of anaphylactic shock as compared with reactions of injections of pollen.

In a recent paper [13] I dealt with a series of reactions following injections of substances other than pollen and serum. It was demonstrated that injections of such antigens as drugs, foods or extracts of bacteria and fungi are likely to produce symptoms identical with those seen after injections of pollen. After an intravenous injection of sodium iodide in one case and methenamine-quinine in another, symptoms of true anaphylactic shock as observed following injections

13. Waldbott, G. L.: Anaphylactic Shock from Substances Other Than Pollen and Serum, to be published.

14. Waldbott, G. L.: Systemic Reactions from Pollen Injections, J. A. M. A. 96:1848 (May 30) 1931.

of pollen and serum occurred. Again, it was shown that a violent allergic reaction and protracted anaphylactic shock cannot be differentiated clinically. Furthermore, it was demonstrated that typical shock may be elicited in other ways than by injections. An additional factor in the production of shock was emphasized: The time interval between two injections may, under certain conditions, greatly enhance the degree of sensitization. This, again, is in accord with the observations in experiments on animals in which the interval between the sensitizing and the shocking dose is of greatest importance.

The clinical and pathologic manifestations of anaphylactic shock are subject to great variations. Perusal of the available literature indicates that the chief pathologic lesions are capillary congestion and edema, with subsequent cellular infiltration. These lesions have been excellently described by Kline and his co-workers [15] in their investigation on the allergic wheal. Recent experiments by Róth and Szauter [16] revealed the following: If the antigen is introduced into the venous system, the capillary circulation of the lungs, which are then first reached by the antigen, becomes principally involved by these changes, as proved clinically by the symptoms of wheezing and dyspnea. Because absorption from an injection takes place almost entirely through the lymph and venous system, the predominance of pulmonary symptoms in anaphylaxis can thus be well understood. If the injection is given into the carotid artery the edema occurs in the brain; convulsions and other cerebral symptoms manifest themselves. If the injection is made into the portal vein, the clinical syndrome of collapse and changes in the function of the liver is most pronounced. This great variability of the symptoms of anaphylaxis is further enhanced when a previous allergic lesion is present (Waldbott [14]). The administration of the antigen usually causes such a lesion to flare up. For example, in the case of a patient subject to allergic migraine headaches (R. N.) cerebral symptoms were produced by an overdose of antigen. In a patient sensitive to pollen, with gastro-intestinal allergy, an overdose of pollen elicited gastro-intestinal spasm, pain and vomiting. Thus, the typical picture of human shock becomes further clouded. In addition, the rapidity of absorption of the antigen is likely to modify the symptoms, inasmuch as death may appear so rapidly following intravenous injections that no symptoms can be noted (Duke,[17] Lamson [18]).

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15. Kline, B. S.; Cohen, M. B., and Rudolph, J. A.: Histologic Changes in Allergic and Nonallergic Wheals, J. Allergy **3**:531 (Sept.) 1932.

16. Róth, I., and Szauter, D.: Experimentelle Beiträge zur Frage der Organanaphylaxie, Klin. Wchnschr. **11**:456 (March 12) 1932.

17. Duke, W. W.: New Method of Administering Pollen Extracts for Purpose of Preventing Reactions, J. A. M. A. **94**:767 (March 15) 1930.

18. Lamson, R. W.: So-Called Fatal Anaphylaxis in Man, J. A. M. A. **93**: 1775 (Dec. 7) 1929.

PATHOLOGY OF SO-CALLED THYMIC DEATH

With these facts in mind, one hundred and two cases of so-called thymic death were studied. One is confronted with the question of what justifies the diagnosis of "thymic death." The work of Young and Turnbull,[1] of Hammar [19] and particularly of Boyd [4] indicates that an "enlarged thymus" is frequently present in any type of sudden death regardless of the cause. I have, therefore, placed less reliance on the degree of enlargement of the thymus, the interpretation of which may be subject to the personal equation, than on the simultaneous presence of a general lymphoid constitution and the absence of any definite lesion to account for death. Of the total number of cases, sixty-eight were eliminated because various conditions (table 1) were found, the presence of which was an adequate cause of death. Thus this study

TABLE 1.—*Causes of Death in Sixty-Eight Cases Excluded from This Study in Which Autopsy Showed "Enlarged Thymus"*

	Number of Cases
Hyperthyroidism	11
Gastro-enteritis	11
Respiratory infections	9
Birth trauma	8
Operations	7
Death from heart failure	6
Infectious diseases	4
Miscellaneous	12
Total	68

differs essentially from that of the English Status Lymphaticus Investigation Committee whose work included all such cases.

The thirty-four remaining cases were grouped into three classes: (1) those in which, aside from the typical lesions to be described, no other contributing incident as cause of death could be determined; (2) those in which minor, usually nonfatal ailments were associated and death ensued; (3) cases in which a syndrome of dyspnea, stridor, fever and collapse developed for several hours or days before death occurred. As I shall show, the pathologic data were quite similar in all three groups. The development of the previously mentioned syndrome in the third group can probably be considered as a part of the whole clinical picture in those cases in which the illness did not terminate immediately after the onset.

19. Hammar, J. A.: The Thymus in Men: The Normal Organ, Ztschr. f. mikranat. Forsch., 1926, supp. vol. 6; II. Das Organ unter abnormalen Korperverhältnissen, ibid., 1929, supp. vol. 16.

REPORT OF AUTOPSIES

With the exception of six adults, all patients were children, the majority being infants. There were fifteen boys and nineteen girls. Most of them had been in perfect health up to the time of death. The

Fig. 1 (case 5).—Typical appearance of lungs with capillary congestion, extravasation of blood cells, areas of edema, emphysema and atelectasis. Low power magnification.

average weights of the thymus were 41.7 Gm. in group 1, 38.3 Gm. in group 2, and 25.6 Gm. in group 3, in which there was a more or less protracted illness. The largest thymuses weighed 85 Gm. in two cases. In two cases (1 and 17) in which previous roentgen therapy (four exposures) had been administered, the glands weighed 38 Gm. and

TABLE 2.—*Group 1, Cases of "Thymic Death" with No Contributory Incident*

Case	History	Thymus	Enlargement of Other Lymphoid Organs	Pressure on Trachea	Petechiae	Edema (with Exception of Lungs)	Suprarenals	Heart	Other Changes	Allergic History	Comment
1. P. F. 6 mos. F	21 days after operation for clubfoot; found dead in bed	8×5×2 cm. 38 Gm.	Tonsils; spleen; intestinal; foci in brain	Definite	Pericardium; epicardium; lungs	Larynx; liver	"Very marked hypoplasia of medulla"	Negative	Excess of chromophils of pituitary	Convalescent serum for measles 1 week previous	Had previous roentgen treatment of thymus
2. H. W. 2 yrs. F	Perfect health; died 2 hours after meal	7×4.5×1 cm. 29 Gm.	Spleen; mesenteric; intestinal; foci in liver	No	Choroid plexus; heart; intestines; aorta; lungs; suprarenals	Brain; cerebellum; stomach; liver; gallbladder; lymph nodes	"Paper thin;" medulla practically absent	Silght dilatation of right side of heart	Fatty changes in liver, heart; aorta hypoplastic	Had eczema	.....
3. B. W. 51 days F	Found dead in bed	7×6×2 cm. 38 Gm.	Spleen; servical; intestinal; mesenteric	Very slight	Pleura; pericardium; thymus	Meninges; brain; larynx	Marked hypoplasia; lipoidosis of cortex	Negative	Acute catarrh of colon	Paternal grandfather had asthma	.....
4. B. G. 2 days F	Found dead	5×4×1.5 cm. 15 Gm.	Intestinal	Slight	Pericardium; lungs; thymus; suprarenals	Spleen; liver; stomach; brain	Marked hypoplasia of medulla	Negative	Fatty degeneration of liver and kidney	Mother had asthma	Typical anaphylactic lungs
5. B. A. 21 mos. M	Perfect health; found dead in bed	64 Gm.	Spleen; mesenteric; intestinal	No	Thymus; spleen	Spleen	Very little medullary tissue	Negative	.....	.....	Brother of patient in case 14
6. S. A. 21 mos. M	Two hours before death, convulsions after taking wine and popcorn; cyanosis	25 Gm.	Spleen; hilus; visceral; foci in myocardium	No	Thymus	Bronchi; esophagus; stomach; choroid plexus	One-half average size	Slight right-sided dilatation	Atelectatic areas of lungs; excess of basophils in hypophysis	.....	.....
7. B. M. 2 mos. M	Perfect health; died 2 hours after meal	50 Gm.	Spleen; intestinal; mesenteric	No	.....	Liver; spleen	"Uniformly small"	Slight dilatation of right side of heart	Degeneration of liver; marked eosinophilia	.....	Marked emphysema in lower portions of lungs
8. B. L. 2½ mos. M	Perfect health; died 3 hours after meal	"Marked hypertrophy"	Spleen; mesenteric	No	.....	Liver; kidneys; meninges	"Hypoplastic"	Negative	Beginning degenerative changes in liver; necrosis of germ centers; eosinophils in ileum, cecum and lymph glands	.....	.....
9. R. A. 5 mos. M	Diarrhea a few weeks; vaccination 4 days; perfect health ½ hour before death	"Marked hypertrophy"	Mesenteric; ileocecal; mediastinal	No	Larynx; pleura	Spleen; kidneys; lymph glands	Generally hypoplastic; small cortical adenomas	Negative	Necrosis of Hassall's corpuscles; eosinophilia in ileum	Negative	.....
10. G. E. C. 4½ mos. M	Found dead in bed	3.5×6×2 cm. 31 Gm.	Spleen; intestinal; mesenteric	No	Lymph glands	Spleen	.....	Slight right-sided dilatation	Marked eosinophilia in various organs	History of continuous "head colds" without fever	.....
11. A. T. 12 yrs. M	Perfect health	8×5×? cm. 85 Gm.	Hilus; mesenteric; foci in liver	No	Lungs; kidneys	Liver; kidneys; spleen; brain	.....	Slight hypertrophy of left side of heart	.....	.....	.....

22 Gm. respectively. Microscopically, there were in all cases hyperplasia of lymphoid organs and exhaustion of the germ centers, as has been described by Symmers.[20] In six instances the presence of necrotic areas in the lymph glands was particularly pronounced. Accumulations of lymph cells were found in the liver, pancreas, heart, brain substance and other viscera.

The most constant and characteristic changes were present in the lungs. On gross examination there was a marked increase in weight and exudation of fluid from the cut surface. Some areas were crepitant, others distended, others edematous. The microscopic sections of all thirty-four cases showed areas of marked dilatation of capillary blood vessels. In some instances the capillaries appeared to be packed with blood cells. In other lesions there was extravasation of blood cells or exudation of edematous fluid into the alveolar spaces and secondary bronchi. In the degree of the advancement of this process, the lung tissue showed various stages of destruction. In the most advanced lesions there was evidence of complete necrosis, the normal tissue being displaced by cellular detritus. Neutrophils, lymphocytes, epithelial cells and, in some instances, eosinophils were present in these lesions. In the less affected parts, the lung tissue seemed to be fairly well preserved, in other areas, entirely normal. Alternating with these changes were areas of emphysema, as indicated by overdistention and rupture of alveolar walls, and areas of atelectasis in various degrees of development. The bronchi usually contained blood or a serous exudate. In a few instances there was a distinct spasticity of the smaller bronchi, similar to that described by Huber and Kessler in asthmatic death.

The lungs of the cases of group 1 and group 2 showed no difference in appearance. In those of group 3, however, in which the "thymic syndrome" had persisted, and fever had been present for several days, a distinct tendency toward organization of these lesions could be noted. Some such areas had the appearance of bronchopneumonic lesions. In case 28, in which the hemorrhagic edematous area had been well outlined, the pneumonic process had partially replaced the former lesion.

Besides the pulmonary changes, there was a notable absence of a definite and constant pathologic process. Capillary dilatation and edema appeared in various other organs, but the extent of these changes was much less pronounced than in the lungs. The localization of the capillary congestion seemed to be subject to great variability. It was present in brain, thymus, liver, kidneys and other organs, as indicated in column 7 of tables 2, 3 and 4. In twelve instances the liver showed a more or less pronounced degree of degeneration. Aside from accumula-

20. Symmers, D.: Status Lymphaticus, Am. J. M. Sc. **156**:40 (July) 1918.

TABLE 3.—*Group 2, Cases in Which Minor Usually Nonfatal Conditions Were Coincident with Death*

Case	History	Thymus	Enlargement of Other Lymphoid Organs	Pressure on Trachea	Petechiae	Edema (with Exception of Lungs)	Suprarenals	Heart	Other Changes	Allergic History	Comment
12 C. A. F. 7 wks. M	Perfect health; after evening meal, short cry; death	32 Gm.	Generalized	No	Epicardium; pleura; thymus	Larynx (slight); brain; liver	Hypoplasia of cortex and medulla	Negative	Slight fatty changes in kidneys; left subacute otitis media; uncomplicated	.....	.....
13 E. D. 48 yrs. F	Diarrhea 4 mos.; sudden collapse; hoarseness; dyspnea	35 Gm.	Lymph tissue of laryngeal mucosa; mesenteric; retroperitoneal; foci in liver	No	None	Liver; spleen	Left suprarenal fibrotic, no medulla; right slightly hypertrophic	Negative	Thyroid adenoma; fibrosis of ovary; healed tuberculosis of lung and pelvic organs	None	.....
14 H. E. A. 3½ yrs. M	Had several convulsions after eating corn; fever several hours before death	25 Gm.	Intestinal; mesenteric; foci in liver	No	Fundus of stomach; lungs; spleen; thymus	Cortex and pia of brain; spleen; kidneys	Small medulla	Slight right-sided dilatation; slight thickening below aortic valve	Dilatation of stomach; marked necrosis of lymphoid germ centers	.....	Brother of patient in case 5
15 A. O. 5 yrs. F	Sudden coma, shock; "rattle" in chest; hoarseness; died after 13 hours	24 Gm.	Throughout gastro-intestinal tract; tonsils; hilus	No	Spleen; lungs; thymus; brain; stomach	Thyroid; lymph glands; bronchi	Moderate amount of medulla present	Slight right-sided dilatation	Cloudy swelling of liver; many eosinophils; healed tuberculous glands	.....	.....
16 P. D. 21 yrs. M	Died during tonsillectomy (local anesthesia)	4.5×12×4.5 cm.; 29 Gm.	Lingual tonsil; cervical; visceral	No	Lungs; lymph glands; thymus	Brain—meninges; spinal cord; pharynx; esophagus; liver; kidneys	"Thinner than normal"	Slight right sided dilatation	Hypoplasia of aorta; fatty degeneration of liver; eosinophilia in various tissues and blood	Allergic rhinitis	.....
17 V. D. 4 wks. M	Died 4 hours after operation for cleft palate	5×3×2 cm.; 22 Gm.	Bronchial; intestinal; spleen; foci in liver	No	Lungs	Kidneys	No record	Slight dilatation of right side of heart	Suprarenals of Marchand in epididymis	Asthma and hay fever in several members of family	Had four roentgen treatments over thymus
18 E. M. 26 yrs. M	Died during appendectomy; no complication	7×8×2 cm.; 41 Gm.	Mesenteric; visceral; thyroid	No	None	Extreme in all organs	Hypoplasia	Marked dilatation of right ventricle	Cloudy swelling and necrosis of liver	.....	.....

19 E. W. D. 5 yrs. M	Died during appendectomy; no complication	7½×7×5 cm.	Gastrointestinal; mesenteric; spleen	No	Thymus; lungs; appendix	Kidneys	General hypoplasia; medulla almost absent	Negative	.....	.....	.....
20 S. V. 2 yrs. F	10 minutes after starting ether anesthesia for operation for cleft palate	39 Gm.	Spleen; gastrointestinal; mesenteric	No	None	Kidneys	"Small, some cortical atrophy"	Negative	Marked eosinophilia in gastrointestinal tract and lungs	Eczema; father had asthma	.....
21 M. H. 37 yrs. F	Frequent colds in nose and chest; joint pains; stopped breathing during tonsillectomy	Not enlarged	Extreme enlargement of lingual tonsil; gastrointestinal; cervical	No	Kidneys	Kidneys	Lipoma in both suprarenals	Negative	Several fatty tumors on thigh; eosinophils in lungs	.....	.....
22 A. R. 26 yrs. F	8 months primipara; severe pain in right side of abdomen and of chest; vomiting; collapse	85 Gm.	Foci in heart; spleen	No	Thymus; epicardium; myocardium	Kidneys	Enlarged; large vessels occluded by thrombi; areas of necrosis	Slight hemorrhages	.....	.....	.....
23 B. L. 16 mos. F	Died 6 hours after second degree burn involving one-fifth of body surface	45 Gm.	Spleen; intestinal; hilus; foci in liver	No	Spleen; thymus; lymph glands; lungs	Small and large intestines; myocardium; spleen; suprarenals	"Medulla almost absent; cortex paper-thin"	Slight dilatation of right side of heart	Aorta hypoplastic; cloudy swelling of liver and kidneys; numerous eosinophils in liver and thymus	.....	Congenital absence of one lobe of lung
24 J. B. 8 yrs. M	Died 2 days after eating poisoned sauer kraut; temperature, 104 F.; vomiting	30 Gm.	Tonsils; hilus; visceral	No	Liver; lungs; suprarenals	Pharynx; brain; liver; spleen; thymus	.....	Slight degenerative changes in myocardium	Fatty degeneration of liver; many eosinophils in stomach and intestines	.....	Five other members of family became ill from same source, but not seriously
25 F. H. 21 mos. F	Vomiting; convulsions for 1 day	"Moderately enlarged"	Intestinal; mesenteric; axillary; inguinal; foci in heart	No	Spleen	.....	Negative	Negative	Fatty degeneration of liver	.....	.....
26 G. C. 1 yr. F	Died 2 days after operation for cleft palate	53 Gm.	Iliac; mesenteric; cervical	No	Stomach	Meninges	No medullary tissue seen in its usual position	Negative	Necrosis of lymph centers in spleen	.....	.....
27 A. M. 4 mos. M	Dyspnea for several weeks; tracheotomy; died immediately after	2 lobes; 5×4×2 cm., 4×3×2 cm.	Cervical; mesenteric	Marked (3 cm. below cricoid cartilage)	.....	Spleen	No pathologic changes	Marked hypertrophy	Marked congestion in lungs; marked eosinophilia	.....	.....

TABLE 4.—*Group 3, Cases Manifesting the "Thymic Syndrome"*

Case	History	Thymus	Enlargement of Other Lymphoid Organs	Pressure on Trachea	Petechiae	Edema (with Exception of Lungs)	Suprarenals	Heart	Other Changes	Allergic History	Comment
28 R. E. M. 2½ yrs. M	Died suddenly after acute infection of upper respiratory tract of 1 day's duration	32 Gm.	Cervical; spleen; gastrointestinal	No	.....	Some laryngeal edema	Lipoidosis of cortex	Small areas of necrosis	Small areas of pneumonia adjoining hemorrhagic tissue; fatty degeneration of kidneys and liver	.....	.....
29 J. M. 21 yrs. M	Infection of upper respiratory tract; dyspnea; cyanosis; died 4 days after onset	50 Gm.	Spleen; mesenteric; intestinal; hilus; foci in heart	No	Thymus; stomach; spleen	Spleen; pancreas; capillary dilatation of heart	"Somewhat thinner than average"	Slight dilatation of right side of heart; some hypertrophy of left	Fatty infiltration of liver and kidneys; areas of suppuration in lungs	.....	Formerly had hyperthyroidism
30 W. L. 6 mos. M	Cough, wheezing; fever 107 F.; death 24 hours after onset	10-12 Gm.	Spleen; mesenteric	No	Lungs	Kidneys; mesenteric vessels	"Very much diminished medullary substance;" extensive dilatation of capillaries	Negative	Necrosis of lymph follicles; necrosis of liver	.....	.....
31 N. E. 3 mos. M	2 weeks previously, pneumonia which cleared up; sudden cyanosis 12 hours before death, followed by 105 F. fever	16.5 Gm.	Mesenteric; hilus	No	Epicardium	Large bowels; kidneys	No note	Negative	Marked emphysema; cloudy swelling of liver; many eosinophils in thymus	.....	.....
32 R. A. R. 4 mos. F	Respiratory infection 2 days, fever 106 F.; stridor; dyspnea	35 Gm.	Bronchial; mesenteric; intestinal	No	Thymus; epicardium; pericardium; lymph nodes	Liver; brain	"One quarter of normal size," necrosis of medullary tissue	Negative	Left ovary larger than right; necrosis of lymphoid germ centers	Negative	.....
33 M. E. H. 10 mos. F	Cough, fever, vomiting, stridor, dyspnea for 2 weeks before death	20.5 Gm.	Mediastinal	No	None	Liver; larynx; bronchi	Negative	Negative	.....	Negative	Had 10,000 U. diphtheria antitoxin and intubation 8 hours before death
34 L. S. 3 mos. M	Occasional cyanosis, vomiting; fever, dyspnea, lung edema 3 hours before death	15 Gm.	Mesenteric; mediastinal; foci in larynx and liver	No	Peritoneum	Spleen; liver; brain	"Small medulla"	Negative	Eosinophilia in liver and spleen; degeneration of liver cells	Sensitive to orange juice; mother had hay fever	Had roentgen therapy of thymus

tion of lymph cells in the capsule of Glisson and some congestion of capillary vessels, there were otherwise no noteworthy findings in the liver.

Petechial hemorrhages were found in the pleura, epicardium, peritoneum and some viscera in twenty-nine cases. The suprarenal glands presented a rather characteristic picture. Regardless of the fact that the findings were recorded by different pathologists, there were notes on the marked hypoplasia of the suprarenals, especially of the medulla, in most records. Descriptions such as "suprarenal glands paper-thin," and "medulla practically absent" had been entered in the protocols. The heart showed neither marked microscopic nor macroscopic pathologic changes except that dilatation of the right ventricle was found in fourteen cases. Hypoplasia of the aorta and heart was noted in a few records. On close examination of the tissues, in some instances, more or less marked eosinophilia was found, especially in the tissues of the gastro-intestinal tract and in the lymph glands.

In only three cases was evidence found of a compression of the trachea by the thymus. In none, however, was there complete obstruction.

INTERPRETATION OF OBSERVATIONS

In summary, the principal and most constant changes occurred in the lungs. Capillary dilatation and edema were found in every case. In most descriptions in the literature on "thymic death" the records indicate that these changes were present; however, pathologists have considered this edema as "passive congestion," and for this reason some have hardly mentioned its existence.

If the edema were of secondary nature one would be able to postulate a primary cause, most likely either a failing heart or, possibly, lesions of the kidneys. It is true that in fourteen cases in which the pulmonary lesions were advanced, a more or less marked dilatation of the right side of the heart was found. However, because this represents only a relatively small proportion of the total number of cases, and because the degree of dilatation corresponds with the extent of the pulmonary changes, I believe that this condition of the heart is secondary to the congestion in the pulmonary circulation: the right side of the heart becomes insufficient for overcoming the additional burden imposed on it by the capillary congestion of the pulmonary circulation. If one considers the edema as the primary lesion, the presence of petechial hemorrhages would indicate that death takes place by asphyxiation as the result of the congestive changes in the lungs.

COMPARISONS WITH ANAPHYLACTIC SHOCK

There are few exhaustive reports of autopsies in cases of anaphylactic shock in the literature. In some, the picture of shock is clouded by the presence of additional pathologic conditions such as diphtheria and asthma. Probably the most thorough description is that of Dean,[21] about a soldier who died seventy minutes after a prophylactic injection of 500 units of tetanus serum. Because the pathologic changes in this case, particularly in the lungs, correspond so closely with the lesions noted in every case of this series, Dean's description of the changes in the lungs is herewith given verbatim:

> The appearance of different microscopical fields shows considerable variation. In many places the alveoli are of normal size, while the capillaries show a moderate degree of dilatation. In other regions the capillaries are dilated and engorged, while the alveoli are more or less flattened and compressed. In hardly any case does this compression amount to complete collapse. Among the flattened alveoli occur here and there alveoli with a round outline, which appear to have been overdistended. In other parts occur groups of alveoli which are much dilated, and in some, rupture of the walls is seen. Irregular dilatation of alveoli and rupture of walls is, however, no very uncommon finding in sections made from post-mortem material. Throughout the lungs, the capillaries are dilated. This dilatation is but little marked in the walls of the more greatly distended alveoli. Where the alveoli are compressed the dilatation is considerable. In a few places minute hemorrhages are seen, and here and there alveoli contain leucocytes and epithelial cells, or are filled with a pink-stained material which probably represents a microscopical degree of edema. The epithelium of the bronchioles is normal in appearance. In a few places the bronchioles appear surrounded by a thin sheath of lymphoid tissue. Many of the capillaries contain a large number of leucocytes.

Table 5 illustrates further the great similarity of the pathology of anaphylactic shock with that recorded here. Hyperplasia of lymphoid tissue, petechial hemorrhages and dilatation of the right side of the heart can be noted, aside from the typical lesions of the lungs.

Further analysis of tables 2, 3 and 4 discloses additional evidence for the substantiation of the anaphylactic theory as the cause of death in cases of thymic death.

1. Eosinophilia of tissues was noted in thirteen cases. Eosinophilia may or may not be present in anaphylactic and allergic lesions. This is demonstrated by Kline and his co-workers[15] who found that the tissue of the allergic wheal, the prototype of the allergic manifestations, does not show eosinophils within the first five to ten minutes after administration of the antigen. Later, eosinophils begin to appear and the maximum of the eosinophilia is reached thirty-five minutes after the injection. Thereupon the number of eosinophils diminishes. While

21. Dean, H. R.: The Histology of a Case of Anaphylactic Shock, J. Path. & Bact. **25**:305 (May) 1921.

there are no definite data available regarding the behavior of eosinophils, in anaphylactic shock, it is noteworthy that among the authors who write on sudden death following injection of serum, quoted in table 5, Dean is the only one who mentions the presence of eosinophils in

TABLE 5.—*Comparison of Author's Pathologic Data with Those on Anaphylactic Shock Reported in the Literature* *

Author	Enlargement of Lymphoid Tissue	Congestion	Petechiae	Lungs	Heart	Other Pathology
Author's Cases						
Waldbott				In all cases: capillary dilatation; edema; hemorrhages; emphysema; atelectasis	Dilatation of Right Heart	
Group 1: 11 cases	11	11	9		5	
Group 2: 16 cases	16	14	13		8	
Group 3: 7 cases	7	5	7		1	
Anaphylactic Shock † (Following Injections of Horse Serum)						
Gurd, Fraser and Roberts: Lancet **1**: 705, 1920	Intestinal	Liver; spleen; stomach; kidney	Subpleural; subepicardial	Emphysema; atelectasis; hemorrhages	Slight dilatation of right side of heart	
Boughton, T. H.: J. A. M. A. **73**: 1912, 1919	.....	Stomach; gallbladder; appendix; liver	Spleen; liver; heart; subperitoneal	Emphysema; hemorrhages; exudation	.....	Asthma
Mendeloff, M. L.: J. A. M. A. **82**: 1862, 1924	Thymus spleen	No record	No record	No record	Aorta small	
Dean, H. R.: J. Path. & Bact. **25**: 305, 1922	Mediastinal; cervical; axillary	Liver–larynx; spleen	.....	Capillary dilatation; edema; emphysema; atelectasis	.....	Eosinophilia
Scheppe, W. M.: J. Lab. & Clin. Med. **16**: 372, 1930	Axillary	Liver; neck; head	.....	Emphysema	"Engorgement of right side of heart"	
Bullowa, J. G. M., and Jacobi, M.: Arch. Int. Med. **46**: 306, 1930	.....	Kidney; brain; suprarenals	.....	Emphysema; capillary dilatation	Right side of heart distended	Diphtheria

* In only 6 of 18 cases reported in the literature were the data sufficient to warrant inclusion in this table.

† Klotz and Gillete each report 1 case, Lamson, 2, of sudden death following injections of serum in which enlargement of the thymus gland is the only outstanding pathologic lesion.

the tissues. In his case there was an interval of seventy minutes between injection and death.

2. In most of our cases it was impossible to check the data of the family and personal history for allergic manifestations. As indicated in tables 2 to 4, there was a positive allergic history in nine of thirteen cases in which such data were obtained. In supplementary clinical investigation by Waldbott and Anthony,[12] a follow-up of thirty children who had formerly been treated with roentgen rays over the thymus gland revealed that all but five were allergic, as determined by skin

tests, and the personal and family history. In three of these five cases sensitization was suggested, but not definitely proved.

3. Eighteen of the thirty-four cases showed changes in the suprarenal glands, chiefly hypoplasia of the medulla. Jaffe [22] and Marine [23] demonstrated that a lack of suprarenal tissue encourages growth of lymphoid tissue. On the other hand, it is generally known that the product of the suprarenal medulla has a marked effect on the allergic wheal. The relationship of pathologic changes in the suprarenal glands to asthma has not been stressed in previous reports of autopsies, with the exception of that of MacDonald. He noted hypoplasia of the suprarenal medulla in death due to asthma.

The syndrome exhibited by the cases of group 3, characterized by dyspnea and collapse, followed by fever and the manifestations of bronchopneumonia, is well in accord with observations made on anaphylactic shock in man. I have records of two patients treated elsewhere; one (M. B.) was in a state of severe shock following an injection of the extract of cotton seed; the other (A. M.) was in a state of shock from pollen extract, fever and pneumonic consolidation developing within a day after the subsidence of the most acute symptoms. The development of similar lesions following severe asthmatic attacks is not uncommon. This probably represents the tendency toward cellular immigration into the edematous lesions and the subsequent organization. Incidentally, the relatively small average size of the thymuses in group 3 as compared with those in groups 1 and 2 can be explained by the presence of a febrile disease, in accord with the well recognized fact (Boyd) that febrile disease reduces the size of the thymus and lymphoid tissue.

MODE OF ABSORPTION OF ANTIGEN

Since we are accustomed to identify with anaphylactic shock firstly a protein or protein-like antigen and secondly a hypodermic injection, and since such a conception would form the foremost objection to the anaphylactic theory of so-called "thymic death," a review of the facts concerning these two questions is necessary.

Through the extensive work of Landsteiner [24] and that of Avery and his co-workers,[25] it has been definitely proved that nonprotein-

22. Jaffe, H. L.: On Diminished Resistance Following Suprarenalectomy in Rats, Am. J. Path. **2**:421, 1926.

23. Marine, D.; Manley, O. T., and Baumann, E. J.: The Influence of Thyroidectomy, Gonadectomy, Suprarenalectomy and Splenectomy on the Thymus of Rabbits, J. Exper. Med. **40**:429 (Oct.) 1924.

24. Landsteiner, K., and Van der Scheer, J.: Serological Differentiation of Steric Isomers, J. Exper. Med. **48**:315 (Sept.) 1928.

25. Tillett, W. S.; Goebel, W. F., and Avery, O. T.: Chemo-Immunological Studies on Conjugated Carbohydrate-Proteins, J. Exper. Med. **50**:551 (Nov.) 1929.

containing substances, formerly termed nonantigens, may be sources of allergic and anaphylactic manifestations. I have reported instances of anaphylactic shock in man following simple nonprotein-containing chemicals [13] and have particularly pointed to the sensitizing effect of local and general anesthetics.[10]

There is sufficient evidence for the belief that shock may occur as the result of absorption of antigen through channels other than injections, provided the three necessary requirements are fulfilled: marked sensitivity of the patient, a dose above the degree of his individual tolerance and a rapid absorption of the antigen. Absorption of the whole antigen may take place through the nose and upper part of the respiratory tract, as shown by Cohen and his co-workers [26] with reference to pollen, and by Ratner [27] to other antigens. Walzer [28] proved that undigested antigen such as food is absorbed wholly through the gastro-intestinal tract. In one of the thirty children previously mentioned, severe shock occurred after a scratch test with walnuts. The epidermis was only scarified, no blood being drawn. The edema began at the site of the test, spread within two minutes throughout the body and was followed by severe asthma and evidence of edema of the upper respiratory organs. This mode of production of shock points distinctly to absorption of antigen from a slightly excoriated epidermis. It was definitely stated by the mother that the child, a breast-fed baby, had never eaten walnuts. If absorption of such a minute amount of walnut powder through the skin produced such violent anaphylactic symptoms, one can safely assume that the ingestion and ensuing absorption of much larger quantities of this food through the gastro-intestinal tract would have had more serious consequences, especially considering the great permeability of the infantile intestinal tract. The question arises whether or not the contact with, and absorption of, food in young children, for which reagins have been transmitted from the mother through the placenta or with the breast milk (Ratner [29]), may thus be responsible for the frequent incidence of this type of death in children because of the great permeability of their mucous membranes. Among clinicians it is not an uncommon experience that particularly

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26. Cohen, M. B.; Ecker, E. E.; Breitbart, J. R., and Rudolph, J. A.: The Rate of Absorption of Ragweed Pollen Material from the Nose, J. Immunol. **18**: 419 (June) 1930.

27. Ratner, B.; Jackson, H. C., and Gruehl, H. L.: Respiratory Anaphylaxis: Sensitization, Shock, Bronchial Asthma and Death Induced in the Gueina-Pig by the Nasal Inhalation of Dry Horse Dander, Am. J. Dis. Child. **34**:23 (July) 1927.

28. Walzer, H.: Urticaria Wheal Formation on Abnormal Skins, Arch. Dermat. & Syph. **20**:277 (Sept.) 1929.

29. Ratner, B., and Greenburgh, J. E.: Congenital Protein Hypersensitiveness, J. Allergy **3**:149 (Jan.) 1932.

young children show, on contact with a certain food or animal, severe anaphylactic symptoms identical with those which occur following injections of pollen and serum. Thus it is likely that anaphylactic shock can be elicited by means other than injection.

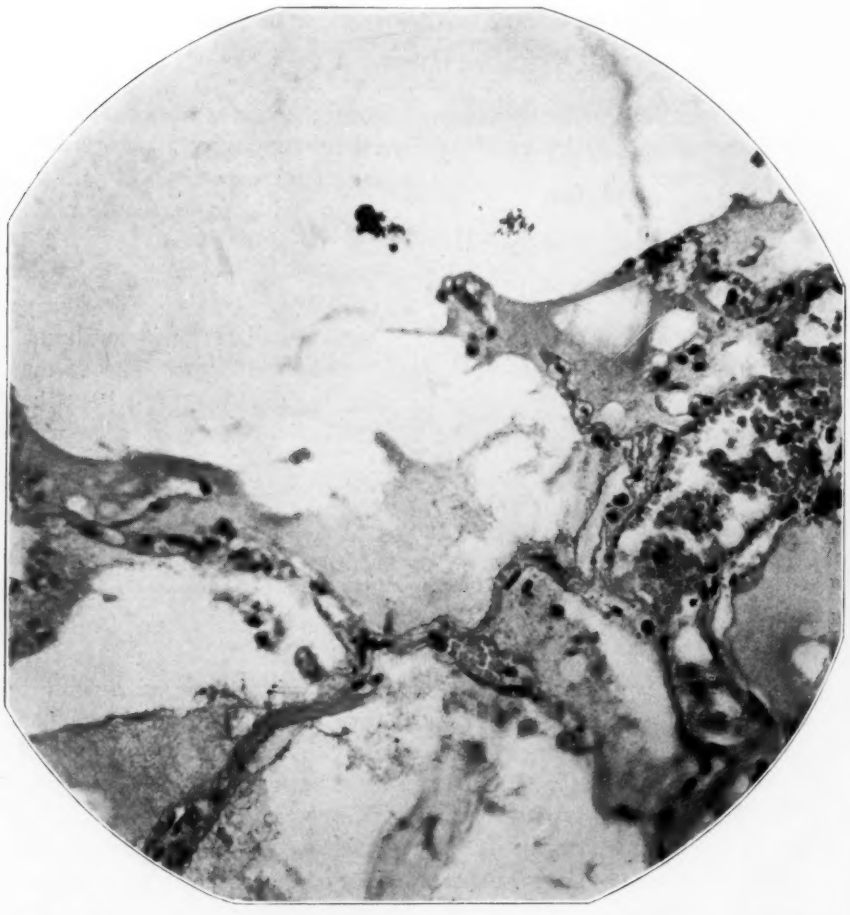

Fig. 2 (case 13).—Stretching and rupture of alveolar walls, capillary congestion and edema fluid. High power magnification.

One of the most unusual cases of my series in which gastro-intestinal absorption of antigen may have played a part is the sudden collapse and death of a woman, 37 years of age (case 13), who had been suffering for three months from mucous colitis, an allergic condition. At the time of collapse severe abdominal tenderness, dyspnea, râles and hoarseness (!) were present. In addition to the pulmonary manifestations which were indicative of anaphylactic shock, the mode of

death suggested this diagnosis because of the aforementioned observation that in anaphylaxis an overdose of an antigen produces a flare-up of a previously existing allergic condition in addition to the other anaphylactic changes. Thus, the symptoms were suggestive of allergic abdominal spasm, pulmonary edema and possibly of edema of the glottis. The autopsy (Dr. P. F. Morse, Harper Hospital) showed marked spasm in the lower intestines, marked capillary congestion and edema of the lungs, an extensive emphysema (fig. 2) and petechial hemorrhages in the lungs. There was a hyperplasia of the thymus (35 Gm.) and of the lymphoid organs, and the characteristic diminution of the suprarenal substance, as noted by other investigators; in this case it was due to a chronic inflammatory process.

RELATIONSHIP OF LYMPHOID TISSUE TO ALLERGY

Among other clinical observations indicating an interrelationship between the lymphoid system and allergy, the following is of interest: The bad effect of removal of lymphoid tissue, as in a tonsillectomy, on asthmatic patients is indisputable among most clinicians. The lymph glands are closely associated with elimination of eosinophil cells from the tissues and blood stream (Biggart [30]). Their rôle of combating foreign material, particularly bacterial infection, is well established. The presence of exhaustion and necrosis of lymphoid germ centers induced Symmers [20] to assume that a toxic substance is deposited in the lymph glands and the thymus. Hammar [19] suggested that Hassal's corpuscles may be the pathologic exponents of an antitoxic function of the thymus.[31] Whatever the facts may be, there appears to exist an intimate association of the lymphoid system with immunologic and allergic processes, the nature of which is not understood.

CONCLUSIONS

1. Of a group of one hundred and two cases in which the diagnosis of status thymicolymphaticus was made by various pathologists, thirty-four were selected in which no adequate cause of death had been determined. Sixty-eight cases were excluded, since other conditions, such as hyperthyroidism, birth trauma, gastro-enteritis and respiratory infections, were associated with lymphoid hyperplasia, and in themselves were sufficient to cause death.

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30. Biggart, J. H.: Some Observations on Eosinophil Cells, J. Path. & Bact. **35**:657 (Sept.) 1932.

31. In children who died from diphtheria after they had had injections of horse serum, Strobl and Wasitzky (Klin. Wchnschr. **12**:1453 [Sept.] 1933) found that the thymus and spleen contained more antibdoies against horse serum than other organs examined.

2. In eleven of the thirty-four cases death occurred without previous illness, nor were there any pathologic lesions to indicate the presence of a previous illness. In sixteen, minor, usually nonfatal incidents preceded death. In seven, a syndrome developed manifesting dyspnea, stridor, fever and shock.

3. The lungs of all these patients presented uniform changes, characterized by capillary congestion, extravasation of blood cells and edematous fluid. These lesions alternated with areas of emphysema and atelectasis. In seventeen cases petechial hemorrhages were present, involving the heart, pleura, lymph glands and various other viscera. In some, there were dilatation of the right side of the heart and degenerative changes in the liver and edema and capillary congestion in other organs than the lungs. Hypoplasia of the suprarenal glands and hyperplasia of the lymphoid organs, as noted by other authors, were present.

4. Comparison of this pathologic process with that reported in anaphylactic shock in man reveals a close resemblance, if not a complete identity, of the two conditions. Eosinophilia of the tissues and an allergic family or personal history point further to this conception.

5. On the basis of these findings it is believed that death may be the result of a primary anaphylactic edema of the lungs and ensuing asphyxiation. Such a theory can be upheld only if one assumes (1) that anaphylactic shock may occur from incorporation into the body of nonprotein substances, and (2) that absorption of shock-producing antigen may take place by ways other than by injections. Evidence is presented, both from personal experience and that of others, which tends to confirm these facts.

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CALCIUM AND PHOSPHORUS STUDIES

VI. OBSERVATIONS ON THE TREATMENT OF LATE RICKETS WITH VIOSTEROL BASED ON THE STUDY OF TWENTY-THREE CASES

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When is rickets to be designated as late rickets? Schmorl [1] writes:

> By late rickets I understand all cases which come under observation in the later periods of growth (after the end of the fourth year). Under the conception of late rickets are to be included, therefore, not only those cases in which the disease began in the earlier growth periods but never disappeared—persistent rickets—but also those cases in which rickets developed for the first time in the later periods of growth—late rickets in the narrower sense. Strictly speaking, only the rickets which first develops in the later growth periods merits the name of late rickets. If, however, I make the conception of late rickets as broad as I do, it is because of the impossibility in many cases of making a clear separation between persistent rickets and late rickets.

Schmorl, therefore, makes age the sole criterion.

Schmorl selects the end of the fourth year as the point of demarcation of late rickets because, as his pathologic studies showed, active rickets becomes relatively infrequent by that time. If one consults Schmorl's table, which gives the incidence of rickets in its varying stages at the different age periods (table 1), one sees that incipient rickets was not found after the second year, and that "florid rickets" [2] had diminished from almost 100 per cent at the end of the first year to

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This study was aided by a grant from Mead Johnson and Company, Evansville, Ind.

From the Harriet Lane Home of the Johns Hopkins Hospital and the Department of Pediatrics of the Johns Hopkins University.

1. Schmorl, G.: Die pathologische Anatomie der rachitischen Knochenerkrankung, Ergebn. d. inn. Med. u. Kinderh. **4**:440, 1909.

2. By "florid rickets" Schmorl means rickets in which the lesions of the disease are in an advanced stage of development and in which no depositions of lime salts have occurred, i. e., advanced rickets without evidence of a tendency toward healing. By "healing rickets" Schmorl means rickets in which depositions of lime salts in the rachitic tissue have occurred, i. e., rickets with evidence of a tendency toward healing. By "healed rickets" Schmorl means cases in which the disease has completely died out but has left in its wake characteristic deformities in the gross or finer structure of the bones.

8 per cent during the fourth year. The table shows also that in the fourth year the percentage of incidence of "healing rickets," 12.5, exceeded that of "florid rickets" [2] and the percentage of incidence of active rickets (that is, including "beginning," "florid" and "healing" and excluding the "healed" [2]) had fallen from almost 100 at the end of the first year to 21 during the fourth year.

It was, then, merely because rickets showed itself to be so much on the wane during the fourth year that Schmorl assigned the end of the fourth year as marking the end of infantile rickets and the beginning of late rickets.

Undoubtedly, the total incidence of rickets in Dresden during the years from 1901 to 1908, when Schmorl made his studies, was far greater than in the corresponding period in American cities. Indeed, the incidence in Dresden at that time must have been greater than at present, since means of prevention have now become so generally

TABLE 1.—*Incidence of Rickets in Its Varying Stages at the Different Age Periods According to Schmorl* [2]

Age, Mos.	Beginning Rickets		Florid Rickets[2]		Healing Rickets[2]		Healed Rickets[2]		Total Number
	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	
2	4	100	..	....	..	....	..	....	4
3	12	75	4	25	..	....	..	....	16
4 to 6	19	57.6	7	21.2	7	21.2	..	....	33
7 to 9	17	34	23	46	10	20.0	..	....	50
10 to 12	7	9.5	45	61.7	20	27.4	1	1.4	73
13 to 18	4	6.9	32	55.2	15	25.8	7	2.1	58
19 to 24	2	6.6	10	33.4	11	36.6	7	23.4	30
25 to 36	..	...	13	22.9	14	24.5	30	52.6	57
37 to 48	..	...	2	8.3	3	12.5	19	79.2	24

understood. Undoubtedly, also under the conditions in the United States, the duration of the disease is shorter than Schmorl's statistics for Dresden would indicate. For example, Park, Eliot and Jackson [3] studied microscopically the skeletons of 141 children aged between 2 months and 5 years, for evidence of rickets; they found, in contrast to the figures of Schmorl, that of children between the fourth month and the second year only from 50 to 60 per cent showed evidence of the disease in active form; that of those between the second and the third year only 10 per cent showed active rickets, and that no children from the fourth to the fifth year showed the active form of the disease. Similarly, when Eliot and Souther,[4] in 1925, made roentgen examinations of the lower ends of the radius and ulna in a group of 1,186 children, including both Negroes and Italians, living in New Haven, Conn., they found that the disease began to become common by the end of the third month, reached its maximum incidence of 47 per cent at the seventh

3. Park, E. A.; Eliot, M. M., and Jackson, D.: Personal communication.

4. Eliot, M. M., and Souther, S. P.: Personal communication to Dr. E. A. Park.

month and then declined in frequency, reaching about 18 per cent at the end of the first year and 4 per cent at the end of the third year. The American statistics therefore indicate that, at the present time, in New Haven and Baltimore, rickets begins to wane at the end of the second year and by the end of the third year becomes reduced to a small percentage. These data suggest that the demarcation point between infantile and late rickets, if Schmorl's approach to the problem is used, should be at about the end of the second or third year. It is to be understood, however, that the boundary separating infantile and late rickets, wherever set, is placed arbitrarily, and that the distinction between infantile and late rickets has in consequence no especial significance. Moreover, chemically and pathologically, late rickets (renal rickets excluded) cannot be distinguished from the infantile type.

Late rickets may be roughly divided as follows: (1) persistent infantile rickets, the infantile disease having persisted either because it was never properly treated or was refractory to therapeutic measures; (2) recurrent rickets, that is, rickets recurring in a child who has recovered from the disease; (3) late rickets in the true sense, that is, occurring for the first time after the third year, sometimes termed juvenile osteomalacia; (4) rickets developing in association with celiac disease, and (5) renal rickets.

Persistent infantile rickets, recurrent rickets and late rickets in the strict sense, so far as we know, are the same disease; they have a common etiologic background in a deficiency of the ultraviolet ray factor in the environment and in the food. Differences in the symptoms, course and extent of the disease are due merely to the variations in the rates of growth in the different parts of the skeleton at different age periods and to the change in the stresses and strains to which the skeleton is subjected during these periods, as in lying, creeping, sitting and standing (Park[5]). Renal rickets, on the other hand, is a totally different condition; it is not a deficiency disease. The faulty deposition of lime salts in the growing parts of the skeleton in renal rickets is due to the failure of the kidney to maintain a normal acid-base equilibrium in the body and to its inability to excrete inorganic phosphorus which may accumulate in the tissue fluids. The attempt on the part of the body to excrete the retained phosphorus through the colon results in the formation therein of an insoluble calcium salt; thus the body is robbed of its available calcium, and the calcification of the growing parts of the skeleton is thereby hindered. Renal rickets, therefore, is a rachitic condition of the skeleton secondary to renal insufficiency. Celiac rickets, the nature of which is not entirely understood, seems to depend on a disturbance in the calcium and phosphorus metabolism

5. Park, E. A.: The Blackader Lecture, "Some Aspects of Rickets," Canad. M. A. J. **26**:3, 1932.

connected with disturbed function of the alimentary tract. It seems possible that the excretion of large quantities of fat may lead to the loss of calcium in the form of soaps, or it may hinder the absorption of calcium and phosphorus or of vitamin D, so that rickets ultimately develops. It must be remembered, however, that in most cases of celiac disease complicated by rickets the patient is in the age period at which rickets is apt to appear in seemingly healthy children, and that during the period of illness the child is usually kept in bed indoors and is deprived of cod liver oil because of its high fat content which, presumably, these children cannot tolerate.

Of these various forms of late rickets, the persistent infantile type is by far the commonest. Recurrent rickets is really the same as persistent infantile rickets. Late rickets in the strict sense, under the conditions which surround children in the United States, is probably exceedingly rare. Hutchison and Shah [6] reported the occurrence of cases of late rickets which were true examples of juvenile osteomalacia in the Mohammedan child wives and in the Hindu wives observing "purdah." But the conditions under which these girls live are rarely duplicated in this country. On entering the matrimonial state the young wives remain indoors and subsist on food lacking vitamin D; the deprivation of the ultraviolet ray factor and the burden of pregnancy predispose them to rickets. Renal rickets occurs not so infrequently. Probably the majority of cases of rickets in white children more than 6 years old are examples of renal rickets, and many of the cases of late rickets reported by Looser [7] may have been of that variety. Celiac rickets is seen in a considerable percentage of young children suffering from celiac disease.

Renal rickets is, of course, little affected by vitamin D therapy or by irradiation with ultraviolet rays from the mercury arc in quartz, and in this form of rickets the treatment with viosterol may be dangerous, if sufficiently pressed. Celiac rickets has been reported to be refractory to cod liver oil therapy. Cases of rickets of the ordinary kind, also, have been reported in which the disease has been refractory to antirachitic agents in ordinary doses (Stearns, Oelke and Boyd,[8] Jampolis and Londe,[9] and Blackfan [10]). We encountered a case of ordinary rickets in a child, aged 4 years, not reported in this paper,

6. Hutchison, H. S., and Shah, S. J.: The Etiology of Rickets, Early and Late, Quart. J. Med. **15**:167, 1921.

7. Looser, E.: Ueber Spätrachitis, Verhandl. d. deutsch. path. Gesellsch., 1905, p. 242.

8. Stearns, G.; Oelke, M. J., and Boyd, J. D.: Mineral Metabolism in Late Rickets, Am. J. Dis. Child. **42**:88 (July) 1931.

9. Jampolis, M., and Londe, S.: The Need of Larger Doses of Viosterol in Severe Rickets (Osteomalacia Type), J. A. M. A. **98**:1637 (May 7) 1932.

10. Blackfan, K. D.: Personal communication to Dr. E. A. Park.

in which the disease was totally refractory to cod liver oil therapy and treatment with ultraviolet rays from the mercury vapor arc in quartz though carried on for months. Since we were aware that in some cases of late rickets the disease is resistant to the weaker forms of medication, we desired to determine whether cases could be found in which the condition was refractory to the most powerful form, namely, viosterol. Accordingly, we assembled from our clinic as many of the older infants and children having advanced rickets as we were able to find, and treated them with viosterol. Altogether we secured 23 children with such a condition. Some of them had already received antirachitic therapy in the form of cod liver oil, but others had received no treatment. One of the patients suffered from rickets complicating celiac disease. None of the patients had renal rickets.

The age, sex, color, previous treatment with cod liver oil, dosage of viosterol, duration of viosterol therapy and results of treatment, as determined in the concentrations of calcium and inorganic phosphorus in the blood and the changes in the skeleton as seen in the x-ray films are tabulated in table 2.

Before therapy was begun, each patient was examined clinically and roentgenologically, and the degree of rachitic activity was roughly estimated. Therapy was continued until the x-ray films showed that the rachitic process had healed completely. In 2 of the patients the moderate doses of viosterol were supplemented by ultraviolet irradiations. In 3 of the patients open osteotomy and in 1 manual osteoclasis was performed at about the end of the therapeutic period; in 3 others manual osteoclasis was done at the beginning. Five of the children showed multiple spontaneous fractures.

REPORT OF CASES

A few of the cases, each selected because of some interesting point, will be discussed in detail.

CASE 6.—N. C., a colored boy, 3⅓ years old, extremely malnourished and weighing only 7,000 Gm., showed the most severe rickets imaginable, which was accompanied by great rarefaction of the skeleton and multiple fractures. The boy was unable even to sit up and had never walked or talked. He had been in the care of an aunt for seven months prior to admission. The diet had been extremely poor, being entirely lacking in milk and green vegetables. Cod liver oil had been prescribed, but there was great doubt as to whether it had been taken. Because of the undernutrition, the extreme rickets and the impossibility of adequate care being given at home, he was admitted to the Harriet Lane wards. At the time of admission, the calcium content of the blood was 8.7 mg., and the inorganic phosphorus, 3.5 mg. per hundred cubic centimeters. Treatment with viosterol (in oil 250 D.)[11] was begun, 20 drops being given daily, and at the same time daily irradiation with ultraviolet rays from the mercury vapor arc in quartz was instituted. In addition, the child now had the benefit of the adequate

11. 250 D = 3,333 Steenbock units per gram.

TABLE 2.—*Essential Data in the Twenty-Three Cases of Our Series*

Case; Name; Age, Years	Color and Sex	Extent of Rickets (Clinical)	Previous Antirachitic Treatment	State of Rickets Prior to Viosterol Therapy (Roentgenograms)	Daily Dosage of Viosterol	Month When Treatment Was Begun	Deposition at Cartilage-Shaft Junction (Stage 1) (Roentgenogram)‡	Lower End of Radius Approximates Normal (Stage 3) (Roentgenogram)‡	Before Viosterol		After Viosterol		Comment
									Calcium, Mg.	Phosphorus, Mg.	Calcium, Mg.	Phosphorus, Mg.	
1 C. F. 2 1/12	C, M	+++	Cod liver oil (3 teasp.) daily from 1½ years to present	Advanced; healing ++†	10 drops (1 yr.)	6	(See comment)	7 mos.	....	...	....	.....	Partial healing already well advanced when administration of viosterol was started
2 H. C. 1 11/12	C, M	++++	Cod liver oil probably taken, but irregularly	Advanced; florid†	10 drops (6 wks.); 15 drops (17 mos.)	5	2 mos.±	8½ mos.	....	...	....	.....	10 drops viosterol, almost no effect; 15 drops, good effect with healing
3 G. S. 2 6/12	C, F	++	Cod liver oil probably taken, but irregularly	Moderately advanced; florid	16 drops (17 mos.)	9	+ 1 mo.	5 mos.	....	...	....	.....	Rapid healing of florid rickets
4 E. L. J. 3	C, F	+++	Cod liver oil probably taken, but irregularly	Advanced; healing +++	15 drops (6 mos.)	13	(See comment)	(See comment)	....	...	....	.....	Healing already extensive; viosterol rapidly completed it
5 M. S. 4 2/12	C, F	++++	Cod liver oil probably taken, but irregularly	Advanced; healing +++	16 drops (1 yr.)	9	(See comment)	(See comment)	....	...	....	.....	Healing already extensive; viosterol rapidly completed it
6 N. C. 3 4/12	C, M	++++	Cod liver oil taken irregularly if at all	Advanced; florid (great rarefaction; multiple fractures)	20 drops (7 mos.) plus daily ultraviolet irradiation (10 weeks)	7	+ 11 days	5 mos.	8.7	3.5	12.9 13.6 9.3	5.2 (21 days) 6.4 (2 mos.) 7.8 (2½ mos.)	Initial deposition at cartilage-shaft junction in 11 days; stage 3 in 5 mos.; then all antirachitic treatment abandoned and rickets recurred (see protocol)
7 D. R. 2	C, F	+++	None	Moderately advanced; florid	24 drops (2 wks.); 30 drops	7	± 2 wks. ++ 1 mo. (1¾ mos.)	2¼ mos.	....	...	....	.....	Viosterol rapidly effected complete healing

8 C. W. 6	C, M	++++	None	Advanced; healing ± florid	20 drops (14 days); 30 drops (7 days); 60 drops (3 mos.)	5	++ 23 days	3 mos. (almost complete); 9 mos. (complete); no films between	....	...	....	.....	Rapid curative effect (for interesting features see protocol)
9 P. C. 1 10/12	C, M	+++	Cod liver oil (3 teasp.) for 1 mo.	Advanced; healing ++	40 drops (4 mos.)	5	(See comment)	3 mos.	....	...	....	.....	Viosterol rapidly completed healing already begun
10 E. A. J. 1 10/12	C, M	++++	None	Advanced; healing ++	40 drops (4½ mos.)	6	(See comment)	1¾ mos.	....	...	....	.....	Viosterol rapidly completed healing already begun
11 B. C. 2 6/12	C, F	++++	None	See comment	40 drops (6 mos.)	5	(See comment)	5 mos.	....	...	....	.....	No roentgenogram taken before viosterol therapy; x-ray film 2 weeks after shows heavy fresh deposits of lime salts; thereafter, rapid healing
12 E. M. H. 2 6/12	W, F	++	None	Moderate; florid	40 drops (9 mos.)	4	+++ 1¾ mos.	3½ mos.	8.1	2.5	9.5 9.1	6.0 (3 mos. 7.4 (6 mos.)	Rapid healing; the rickets accompanied celiac disease (see protocol)
13 R. D. 2 6/12	C, F	+++	Cod liver oil probably taken, but irregularly	Advanced; healing ++	60 drops (7 mos.)	12	++ 1 mo.	5½ mos.	12.1	4.9	12.5	(5½ mos.)	Rapid healing
14 H. A. C. 2 8/12	C, M	+++	None	Advanced; healing +++	60 drops (6 mos.)	7	++ 1 mo.	6 mos. (probably earlier)	....	...	....	.....	Viosterol rapidly completed healing
15 L. O. 2 7/12	C, F	++++	Cod liver oil undoubtedly taken, but irregularly	Advanced; florid,(great rarefaction, multiple fractures)	20 drops (3 wks.); 60 drops (6 mos.)	4	+++ 6 wks. (healing about half complete)	4¼ mos.	9.4	4.2	10.5 10.7 13.7	5.0 (20 days) 5.7 (2 mos.) 5.7 (7 mos.)	Rapid healing; viosterol discontinued at end of 7 mos. because of moderately high calcium in blood serum, although there were no clinical signs of ill effects
16 E. M. 1 8/12	C, F	++++	None	Advanced; florid (great rarefaction, multiple fractures)	60 drops (4¾ mos.)	10	++ 19 days	1⅔ mos.	....	...	12.4	5.9 (1¾ mos.)	60 drops daily caused heavy precipitation at cartilage-shaft junction and throughout rachitic intermediate zone in 18 days; very rapid healing followed

* Immediately preceding treatment with viosterol.

† Florid is used in Schmorl's sense to denote rickets without a trace of lime salt deposition at cartilage-shaft junction of rapidly growing bones; + means that lime salt deposition at cartilage-shaft junction is slight; ++, moderate; +++, considerable.

‡ As pointed out in the text, these time criteria of calcification and repair are indefinite, variable and, consequently, not strictly accurate. At best they give a fairly reliable impression concerning the rate of healing.

TABLE 2.—*Essential Data in the Twenty-Three Cases of Our Series—Continued*

Case; Name; Age, Years	Color and Sex	Extent of Rickets (Clinical)	Previous Antirachitic Treatment	State of Rickets Prior to Viosterol Therapy (Roentgenograms)	Daily Dosage of Viosterol	Month When Treatment Was Begun	Deposition at Cartilage-Shaft Junction (Stage 1) (Roentgenogram)	Lower End of Radius Approximates Normal (Stage 3) (Roentgenogram)‡	Before Viosterol		After Viosterol		Comment
									Calcium, Mg.	Phosphorus, Mg.	Calcium, Mg.	Phosphorus, Mg.	
17 F. S. 3 7/12	C, F	++++	None	Advanced; florid (great rarefaction, multiple fractures)	60 drops (6 mos.)	8	+ 12 days (just perceptible)	6 mos.	....	...	9.1	5.9 (2 mos.)	Initial effect of viosterol rapid, but healing thereafter slow
18 F. B. 3 6/12	C, M	++++	Cod liver oil (3 teasp.) daily from early infancy to present	Advanced; healing ++	40 drops (1 mo.); 60 drops (6½ mos.)	10	(See comment)	4¾ mos.	....	...	12.7	5.5 (6 mos.)	Cod liver oil had presumably checked the rickets but failed to bring about healing; viosterol quickly ended progress of disease
19 E. S. J. 3 1/12	C, M	+++	None	Advanced; florid (trace healing ?)	20 drops (8 mos.); 30 drops (1 mo.); 60 drops (13 mos.)	6	+++ 3 wks.	16 mos.	9.6	2.3	11.2 8.1 8.8 11.4 12.3 12.0	4.6 (18 days) 7.6 (8 mos.) 4.9 (9 mos.) 4.4 (11 mos.) 3.1 (15 mos.) 4.2 (19 mos.)	20 drops viosterol caused heavy precipitation of lime salts at cartilage-shaft junction in 3 wks., but failed to bring about healing in 8 mos.; 60 drops viosterol slowly but surely effected healing (see protocol and table 3)
20 E. T. J. 7	C, M	++++	None *	Advanced; florid (great osteoporosis)	60 drops (12½ mos.)	6	+ 25 days	8½ mos.	12.2	...	9.1 9.6	5.2 (4¼ mos.) 6.0 (8 mos.)	Healing somewhat slow
21 L. T. 6	C, F	++++	None	Advanced; healing +++	40 drops (2½ mos.)	6	(See comment)	3 wks.	....	...	10.6	5.6 (3 wks.)	When viosterol was begun, healing was already advancing slowly; this explains why "stage 3" was so quickly attained
22 F. A. 10	W, F	+++	None *	Moderately advanced; healing ++	21 drops (1½ mos.) plus ultraviolet irradiations (1½ mos.+)	1	+ 45 days (very slight)	.....	10.2 9.7	2.6 2.3	9.6 9.4	3.2 (15 days) 2.9 (40 days)	The small dose of viosterol had only slight effect; rickets was not healed in this case, but dosage of viosterol employed was small
23 M. L. B. 5	C, F	+++	Cod liver oil probably irregularly for 2 yrs.	Advanced; moderate rarefaction; healing +	30 drops for 10 wks. and 5 wks.; 4 month interval when not taken	5	Advanced healing in 6 wks.	Viosterol taken for 10 wks., then taking lapsed for 4 mos. at which time rickets was nearly healed; completely healed 5 wks. after resuming viosterol	....	...	....	.....	Mentally defective child; inadequate diet and antirachitic therapy (see text)

hospital diet. The x-ray pictures taken after the child had been eleven days in the hospital showed evidence that healing had begun. At the end of three weeks, the calcium was 12.9 mg. and the inorganic phosphorus 5.2 mg. per hundred cubic centimeters. In the x-ray picture taken at the end of four weeks, the shadows of fresh deposits of lime salts in the provisional cartilage a short distance away from the ends of the shafts were distinctly visible. At the end of two months, the serum calcium was 13.6 mg. and the inorganic phosphorus 6.4 mg. per hundred cubic centimeters. Because of the moderate hypercalcemia, irradiation was withdrawn but the administration of the viosterol was continued. At the end of two and one-half months, the x-ray pictures showed the healing process to be far advanced; the serum calcium at this time was 9.3 mg. and the inorganic phosphorus 7.8 mg. per hundred cubic centimeters.

Because of the relatively high level of the inorganic phosphorus, the treatment with viosterol was also stopped, and the child was discharged from the hospital. Through one of the social agencies the diet at home was supplemented with milk. Cod liver oil was taken, but only for three weeks, after which there was no antirachitic treatment. X-ray pictures taken five months after the patient's discharge from the hospital showed the rachitic process to be practically at an end, though the deformities and the periosteal thickenings were still plainly visible. The x-ray pictures taken two months later, however, showed that the rickets had begun again.

The case illustrates recovery by means of viosterol therapy followed by relapse soon after the treatment was discontinued and the child returned to the poor dietary and hygienic conditions prevailing at home.

CASE 8.—C. W., a colored boy, 6 years old, was breast fed for ten months. He began to walk and talk at the age of 1 year. Shortly afterward, however, at 18 months, signs of intracranial disease appeared; the child began to have recurring convulsive seizures, hemiplegia and mental deterioration, so that he became a low grade imbecile. After weaning, the child received milk and the diet of the family table, but at 2 years of age the milk, which was the only considerable source of lime salts, was discontinued. The child had never received antirachitic treatment. He had remained indoors all the time, probably because he could not care for himself outside.

At the age of 6 years the child came under medical observation for the first time. Hemiplegia, mental retardation and signs of advanced rickets were noted. The x-ray films of the extremities showed great thickening of the shafts, an outward bend of the humerus just above the insertion of the deltoid and a backward bend of the lower end of the femur. The cortices of the long bones exhibited the characteristic appearance of lamellation, with narrowing of the marrow cavity. The lower ends of the radius and ulna showed well marked crater formations with considerable fringing, but with scattered deposits of lime salts, denoting the presence of a tendency toward healing. The intervals between the craters and the nuclei of ossification of the epiphyses were well marked (fig. 1*A*). Viosterol treatment was instituted at once as follows: 20 drops a day for two weeks, 30 drops for the following week and 60 drops a day for the ensuing two months. Twenty-three days after the beginning of viosterol therapy, fresh lime salt deposits had become plainly visible in the proliferative cartilage at the ends of the shafts. Two months later the x-ray films showed that all the rachitic tissue of the intermediate zone had become fully impregnated with lime salts, for the still greatly enlarged ends of the radius and ulna were now clearly outlined, and the end of the radius appeared to be in contact with the nucleus of ossification of the epiphysis. Three months after the beginning of viosterol therapy,

calcification seemed to be complete, though the signs left by the disease were still apparent in the finer architecture of the bones (fig. 1 *B*). At this time, approximately three months after the beginning of viosterol therapy, the child was removed from our observation and was not brought back for six months, during which time all antirachitic therapy was suspended. Nevertheless, the x-ray picture taken on the occasion of the return indicated that the rachitic process had not recurred. The lower ends of both radius and ulna appeared to be of normal configuration, although they were still somewhat bulky.

This case is of especial interest because of the striking effect of viosterol in a 6 year old child suffering from severe rickets. The healing process occurred at about the same rate as that commonly seen in the infant treated with cod liver oil. The case also illustrates how a mental defect often modifies environmental

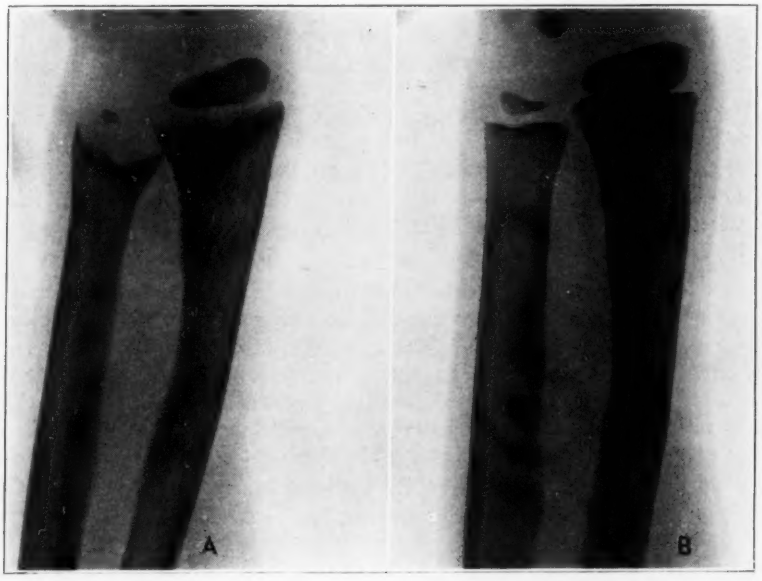

Fig. 1 (case 8).—Severe, chronic rickets in a mentally defective child, aged 6 years, rapidly brought to an end by treatment with viosterol. *A* shows the condition at the beginning of viosterol therapy; *B*, the condition three months later, in which time the healing had become complete.

factors in such a way as to lead to rickets. The child, unable to shift for himself outdoors, was kept indoors except in the evening, when his parents returned from work and carried him out. In addition, the diet was deficient in calcium and phosphorus. In this case, therefore, it is unnecessary to seek for an unusual intrinsic cause to explain the persistence of rickets. Since the rickets developed while the child was deprived of the ultraviolet ray factor, the prompt response to viosterol therapy is not surprising. Doubtless the rickets would have yielded also to cod liver oil.

CASE 23.—M. L. B., a colored girl, aged 5 years, presented rickets similar etiologically to that in the preceding case. In this instance, also, mental retardation, poor diet and confinement indoors contributed largely to the persistence of

rickets from the age of 20 months, when it was first diagnosed, until the age of 5 years. Subminimal doses of cod liver oil were given irregularly during a period of two years prior to viosterol therapy, and slight evidence of healing of the rachitic process was detectable by roentgenologic study. After six weeks of treatment with viosterol, 30 drops being given daily, advanced healing was evidenced by the x-ray films. The administration of viosterol was continued for about a month, thereafter the child did not return, and vitamin D therapy was suspended for a period of four months. On her return, six months after viosterol therapy was begun, the x-ray pictures of the bones showed that the rickets had nearly completely healed. Viosterol therapy was resumed, and the x-ray pictures taken five weeks later showed that complete healing had taken place.

CASE 12.—E. M. H., a white girl, 2½ years old, whose condition had been diagnosed as celiac disease and rickets, chiefly presented an inability to walk, pallor, an enlarged abdomen and large, frothy, pale, offensive stools. Physical

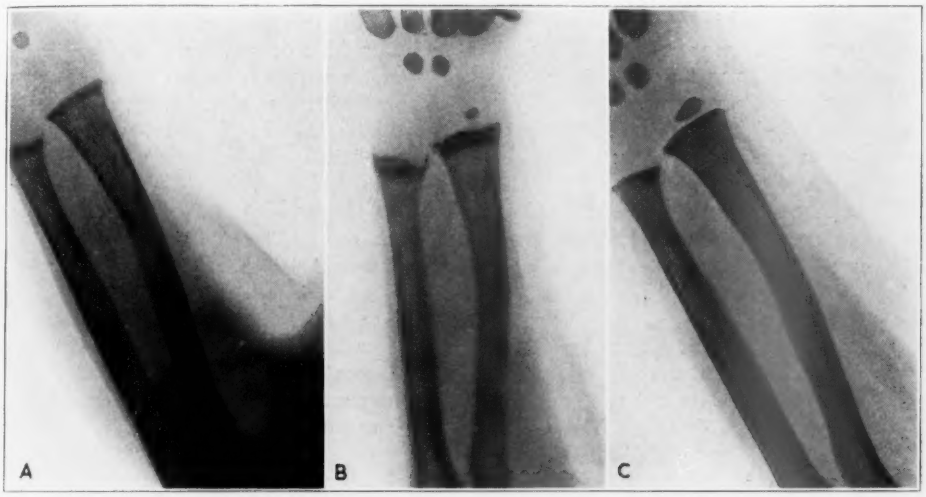

Fig. 2 (case 12).—Rickets complicating celiac disease, but responding rapidly to a dosage of 40 drops of viosterol daily. *A* shows the condition before treatment; *B*, five weeks afterward; *C*, three and a half months afterward.

examination revealed rickets of the chest and extremities, low weight, undernutrition, anemia and a large, protruding abdomen. The stools were typical of celiac disease. The x-ray film recorded rickets and osteoporosis (fig. 2*A*). The abnormal distance between the lower end of the tibia and the nucleus of ossification of the epiphysis gave telltale evidence that the proliferative cartilage was abnormally broad and the rickets more advanced, than the rather slight cupping and fringing indicated. Examination of the blood serum showed calcium, 8.1 mg., and inorganic phosphorus, 2.5 mg. per hundred cubic centimeters. The child was given 40 drops of viosterol daily and a diet high in milk protein, supplemented with bananas. She gained 1,800 Gm. in five weeks and 2,000 Gm. more in the succeeding nine weeks. Under the influence of the diet the stools improved and at the end of three months appeared normal; under the viosterol therapy healing of the rachitic process progressed rapidly. As shown in the x-ray film taken five weeks after the beginning of treatment, unsuspected new ends of the radius and ulna had

made their appearance (fig. 2 *B*). After three and a half months healing had become complete (fig. 2 *C*), and x-ray pictures of the radius and ulna showed that each had grown 2 cm. during this period. After six and one-half months the roentgenographic appearance of the bones had become entirely normal and, except for indistinct zones of increased density at the points in the shaft which marked the rachitic area when therapy was begun, the existence of previous rickets would not have been suspected. Eleven months after therapy was begun, the child had gained 6,400 Gm. and was in perfect health. She was placed on an ordinary diet, without a recurrence of either the celiac disease or the rickets.

CASE 18.—F. B., a colored boy, 3½ years old, suffered from advanced rickets. He was born at full term and was never breast fed. The presence of rickets was suspected at the age of 6 weeks but was not proved until the child was 1 year and 2 months of age, when the x-ray picture showed the disease to be present in an active form. By the age of 2½ years the signs of rickets had become extensive. The child could crawl, but could not walk. When he first appeared in the clinic at the age of 3½ years, and the treatment with viosterol was begun, he presented advanced rickets. There were typical rachitic deformities of the head and great enlargement of the costochondral junctions and of the cartilage-shaft junctions of the wrists, ankles and knees. There was also marked bowing of the legs. The child had suffered from a series of illnesses, an attack of severe diarrhea, acute bronchitis, pertussis, with postpertussis pneumonia, influenza and otitis media, but in spite of this he remained well nourished, weighing 13,500 Gm. at the age of 1⅔ years, and 15,500 Gm. at the age of 3 years.

There is one additional important fact in this case: The child had received cod liver oil in doses varying from 2 to 3 teaspoonfuls daily the greater part of the time from early infancy to the age of 3½ years. The x-ray films taken at different ages previous to the patient's admission to the clinic for rickets are exceptionally interesting as bearing on the influence of cod liver oil therapy. The films taken at the age of 1½ years (fig. 3 *A*) showed active rickets at the lower ends of the radius and ulna without evidence of counter-rachitic tendency in the form of fresh deposits of lime salts along the cartilage-shaft junctions. Those taken at the age of 2½ years (fig. 3 *B*), one year later, showed that while the cupping and fraying at the lower ends of the two bones had become more extensive, scattered deposition of lime salts had occurred in the rachitic intermediate zone bordering on the cup. The films taken at 2 years and 10 months showed that the rickets had become even more extensive, that the deformities of the cartilage-shaft junctions and of the shaft had increased, but that the healing tendency had gained further ground, for the fresh deposits of lime salts at the junction of cartilage-shaft had become heavier and the adjacent ends of the shaft had begun to assume a ground glass appearance. The films taken at 3½ years, when the viosterol therapy was begun, indicated that the healing tendency had assumed a preponderance over the rachitic tendency, as the ends of the bones, though greatly cupped and frayed, had become heavily impregnated with irregular deposits of lime salts.

On admission to the clinic the child was given 40 drops of viosterol daily. The x-ray films which were taken one month later showed that healing was in progress, because the large craters formed by the lower ends of the radius and ulna had become almost completely outlined by heavy deposits of lime salts. The dosage of viosterol was then increased to 60 drops daily. The x-ray films taken one month later (two months after the beginning of viosterol therapy) revealed that the deposition of lime salt was nearly complete. The x-ray films taken three and three-fourths months after the beginning of viosterol therapy indicated that the rachitic

process was at an end, although the abnormal patterns in the finer architecture of the bone, the irregular thickenings of the cortex and the bends seemed more conspicuous than ever. The last films, taken seven and a half months after the beginning of viosterol therapy (fig. 3 *C*), showed that the rickets was at an end. The lower ends of both radius and ulna had become more slender and were losing their bell-like shapes. It was thought that the rachitic deformities might correct themselves sufficiently, so that operative procedure was not advised.

This case demonstrates clearly that though the administration of cod liver oil in the dosage given had not prevented the development of the rickets, it had extended a curative influence, because the healing became steadily more apparent as the child grew older. Probably in time the cod liver oil would have brought the rickets to an end. The viosterol, on the other hand, given in doses of 40 and, later, 60 drops, put an end to the activity of the rickets within a few weeks. All told this patient had been on viosterol treatment in the doses mentioned for seven

Fig. 3 (case 18).—Rickets in a 3½ year old colored boy, which had proved partially refractory to treatment with cod liver oil, but yielded promptly to 40 and then 60 drops of viosterol. *A*, the lower ends of the radius and ulna at 1½ years of age, after prolonged treatment with cod liver oil. Note that the rickets is florid, without any sign of healing. *B*, lower ends of the radius and ulna at 2½ years of age. The rickets has become more extensive; the cupping, fringing and thickening of the bones have increased. With the advance in the rickets in an anatomic sense, however, a healing tendency, doubtless induced by the continued cod liver oil therapy, has declared itself in the form of fresh deposits of lime salts along the end of the fringe in the ulna. *C*, the lower end of the radius and ulna when the child was 4 years and 2 months of age, after viosterol had been given for 7½ months in a dosage of 40 and then 60 drops.

and a half months, without any ill effects becoming apparent. At the end of this period, the serum calcium was 12.7 mg. and the inorganic phosphorus 5.5 mg. per hundred cubic centimeters.

Case 19 (table 3).—E. S. J., a colored boy, 3 years and 1 month old, when first seen in the Harriet Lane Home dispensary, showed enormous enlargement of

TABLE 3.—*Progress in the Treatment of Obstinate Rickets with Viosterol (Case 19, E. S. J.*)*

Date	Treatment	Weight, Gm.	Height, Cm.	Chest, Cm.	Head, Cm.	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Roentgen Changes and Comments
4/20/29	.....	11,000	73.5	48.4	46.0	....	....	Advanced rickets of florid type without any sign of fresh lime salt deposition
6/12/29	Osteoclasis	.....	....	....	....	....	....	
6/22/29	Viosterol, 20 drops	.....	....	....	....	9.6	2.3	Same as on April 20
7/10/29	Viosterol, 20 drops	.....	....	....	....	11.2	4.6	Fresh deposits of lime salts denoting beginning healing have appeared at cartilage-shaft junctions
9/28/29	Viosterol, 20 drops	.....	....	....	....	9.7	....	Five x-ray pictures were taken from 7/10/29 to 5/23/30; all show exactly the same picture of smoldering rickets, characterized by cupping, fringing and irregular, scanty deposition of lime salts at the cartilage-shaft junction; treatment has merely changed the condition from complete rickets (no lime salt deposition at the rapidly growing cartilage-shaft junctions) to a partially healing rickets (40 per cent lime salt deposition at the rapidly growing shaft junctions) without being able to bring about complete healing; the radius, growing steadily during this period, has lengthened exactly 1 cm.
10/18/29	Viosterol, 20 drops	12,000	....	....	....	10.4	....	
11/21/29	Viosterol, 20 drops	12,000	....	....	....	12.6	....	
2/18/30	Viosterol, 20 drops	.....	....	....	....	8.6	7.6	
2/24/30	Viosterol, 30 drops	.....	....	....	....	....	....	
3/19/30	Milk, 1 qt. (946 cc.)	.....	....	....	....	8.8	4.9	
4/ 9/30	Viosterol, 60 drops; milk, 1 qt.	.....	....	....	....	....	....	
4/24/30	Viosterol, 60 drops; milk, 1 qt.	.....	....	....	....	9.7	6.2	
5/23/30	Viosterol, 60 drops; milk, 1 qt.	.....	....	....	....	11.4	4.4	A marked change; lime salts have fallen heavily so that the ends of the shafts are now fully outlined but are still irregular
6/23/30	Viosterol, 60 drops; milk, 1 qt.	.....	....	....	....	....	....	Calcification progressing and ends of bones beginning to approximate normal appearance
9/ 9/30	Viosterol, 60 drops; milk, 1 qt.	.....	....	....	....	12.3	3.1	Calcification almost complete
10/24/30	Viosterol, 60 drops; milk, 1 qt.	.....	....	....	....	12.0	4.2	Calcification virtually† complete
1/24/31	Viosterol, 60 drops; milk, 1 qt.	15,000	86.0	54.0	51.5	....	...	Calcification virtually† complete
2/14/31	Viosterol, 60 drops; milk, 1 qt.	.....	....	....	....	....	....	
5/27/31	Viosterol, 60 drops; milk, 1 qt.	15,100	89.0	....	....	12.2	4.3	

* The patient, a colored boy, 3 years old, had advanced rickets of the florid type at the time when the treatment with viosterol was begun. The dosage of 20 drops of viosterol daily produced within eighteen days a sharp reaction of healing at the cartilage-shaft junctions in the form of heavy deposits of lime salts. However, this dosage proved entirely insufficient to bring about complete healing, for during the eight months of its administration the disease remained in the same stationary state of partial development, the rachitic and the healing processes going on simultaneously. When the dosage of viosterol was finally increased to 60 drops and milk supplied, the final healing began promptly and became complete, though it proceeded somewhat slowly. Under the dosage of 60 drops of viosterol and the administration of milk, the inorganic phosphorus concentration in the serum assumed a value near the borderline of rickets and the calcium concentration rose to 12 mg. per hundred cubic centimeters of blood.

† The word "virtually" is used because even in the last picture taken, thirteen months after the beginning of the treatment with 60 drops of viosterol, we cannot be certain that a trace of rickets is not still shown to be present.

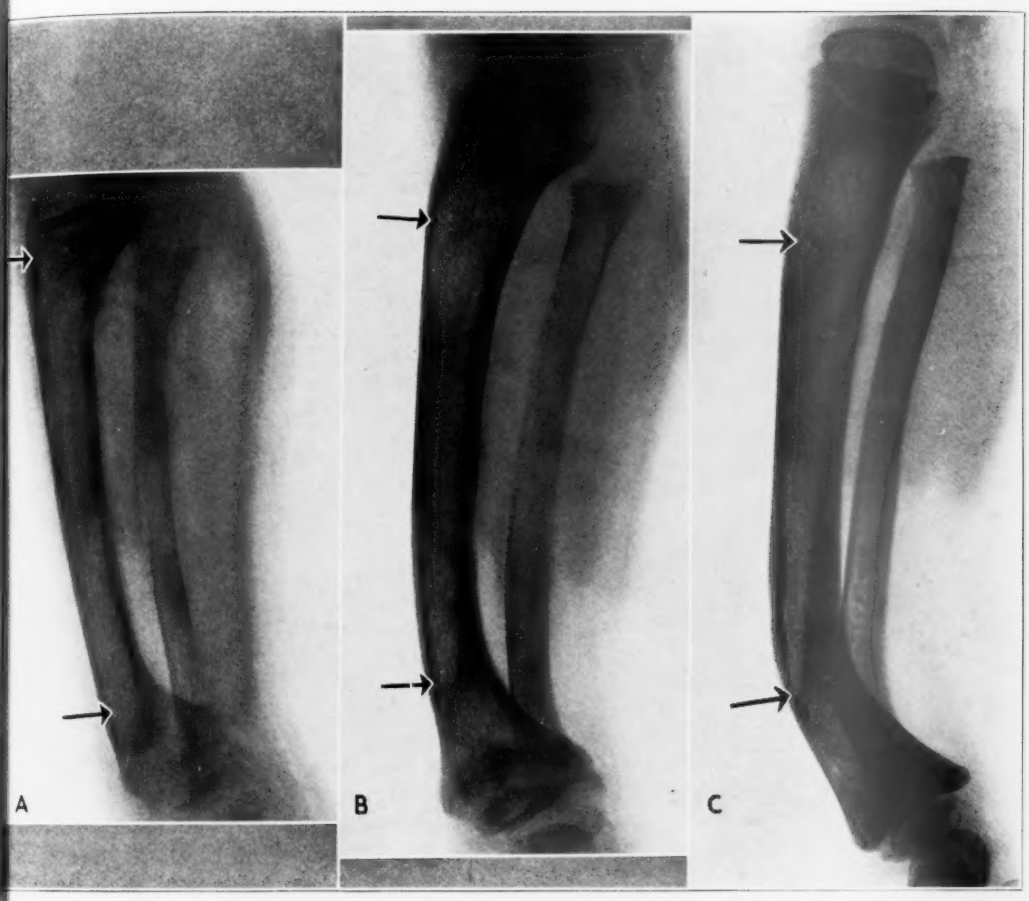

Fig. 4 (case 19).—The effect of viosterol and the continued development of the saber-shin deformity in a colored boy 3 years old showing extreme rickets. *A* shows the tibia one month before the osteoclasis was performed for the correction of the saber shin and the viosterol therapy begun. Note the extreme degree of the rickets without any sign of healing. The arrows indicate the ends of the shafts which antedated the development of the rickets. *B* was taken eleven months after *A*, nine and one-half months after the osteoclasis was performed and eight months after the treatment with 20 drops (one month with 30 drops) of viosterol daily was begun. The ends of the bones show the combination of healing and active rickets. The 20 drops of viosterol have checked the rickets but have been unable to bring about the final healing. Note, also, that the saber-like deformity has increased. *C* was taken five months after *B*, and four and one-third months after the daily administration of 60 drops of viosterol had been commenced. Note that healing is essentially complete, and that the saber-shin deformity has progressed. Arrows indicate the location of the ends of the shaft at the time when the rickets began.

the epiphyses, marked deformities of the lower extremities and roentgen signs of severe rickets (fig. 4). The weight was 11,000 Gm.; the height, 73.5 cm. The child had been fed breast milk for two years, with supplements of cereal and vegetables. No cod liver oil had been given. He sat up at 5½ months and walked at 2 years. The x-ray films taken when he was 3 years old, showed the rickets to be extreme and of the florid variety (fig. 4 *A*). When he was 3¼ years old, manual osteoclasis for the correction of the deformities of the legs was performed; at this time the rickets was still active. Ten days after the operation the serum calcium was 9.6 mg. and the inorganic phosphorus 2.3 mg. per hundred cubic centimeters. Treatment with 20 drops of viosterol daily was then begun. Eighteen days later the serum calcium was 11.2 mg. and the inorganic phosphorus 4.6 mg. per hundred centimeters. After eight months the viosterol was increased to 30 drops daily and in another month to 60 drops. The increase in the dosage of viosterol was prompted by the slowness of the healing, for the rickets, as judged from the x-ray film, had remained in exactly the same state of partial healing for the entire period of eight months. The increase was also prompted by the discovery that the patient's serum calcium concentration was below normal. At three and a quarter months, four months and five months after the institution of the viosterol therapy, the concentrations of calcium in the blood serum had been 9.7, 10.4 and 12.6 mg. per hundred cubic centimeters, respectively. At this time, eight months afterward, the serum calcium was 8.6 mg. and the inorganic phosphorus 7.6 mg. On inquiry it was found that the child had not been receiving milk, and it seemed possible that the low level of the serum calcium and, perhaps, the slow healing were connected with the deficiency of lime salts in the diet. Accordingly, not only was the viosterol increased, but a quart of milk (946 cc.) was provided daily. These changes in treatment gave marked impetus to the healing process.

The film taken one and a half months later showed that since the initial institution of viosterol growth (indicated by arrow in fig. 4 *B*) had been extremely rapid, and that the rickets had changed from the florid state to one in which the healing tendency was pronounced. At the cartilage-shaft junctions the cupping and fringing were exceedingly marked, and yet the signs of abundant, irregular deposits of lime salts were also evident. It is also apparent that during the period of incomplete healing induced by the insufficient dosage of viosterol, the bending deformities had become accentuated. Five months after the increase in the dosage of viosterol the lower end of the radius had assumed an approximately normal appearance. It is interesting that as the healing improved under the large dosage of viosterol the inorganic phosphorus of the serum remained at borderline levels while the concentration of calcium was at high normal levels (table 3).

It is noteworthy that although the daily 20 drops of viosterol produced rapidly (within eighteen days) a healing reaction at the junction of cartilage and shaft in the form of a heavy deposit of lime salts, that dosage failed to bring about a cure during the ensuing eight months. What the daily 20 drops of viosterol really accomplished was to change the rachitic state from one in which apparently no deposition of lime salts was taking place to one in which about 40 per cent of the normal deposition was occurring, at which stage of partial healing the rickets remained. When, however, the daily dosage of viosterol was increased to 60 drops, and was supplemented by the increased supply of calcium and phosphorus furnished in the milk, the rachitic state was again shifted, this time, to one of complete healing.

Osteoclasis was performed in this case before viosterol therapy was begun. Because the rickets did not heal rapidly enough, the legs remained soft and the

deformities corrected by operation recurred. If 60 drops had been given daily immediately after the operation, healing would have taken place rapidly and the legs might have acquired sufficient rigidity to have withstood the strain of walking. In case 13, 60 drops of viosterol was given daily soon after the osteoclasis. A rapid and complete recovery occurred.

CASE 20.—E. T. J., a colored boy, 7 years old, was referred to us from the University Hospital because of our known interest in rickets. The child was a twin; the other died in infancy. He was breast fed for nine months. From the time of weaning, the diet consisted of milk and food from the family table, including eggs and green vegetables but not meat. The child sat up at 8 months; it was said that he learned to walk but soon lost the power and did not walk again until he was more than 4 years old, and when at the age of 7 he was seen by us he was said to be unable "to stand up long or to walk right." The mother had given the child a dessertspoonful of cod liver oil three times a day from the age of 1½

Fig. 5 (case 20).—Roentgenograms of the extremities of a colored boy, aged 7 years, with most extreme rickets and osteoporosis, cured somewhat slowly by viosterol in a dosage of 60 drops daily. *A*, the lower ends of the radius and ulna, showing the most marked rickets without evidence of a tendency toward healing; *B*, the same bones, after two and two-thirds months of treatment with 60 drops of viosterol daily; *C*, the same bones after eight and one-half months of treatment.

to 3½ years. When the boy was 4 years old, he was seen for the first time in the outpatient department of the University Hospital. The following note was made at that time: "extraordinarily rachitic; enlarged joints, stunted body with weak limbs and huge abdomen, enlarged parietal bones, rachitic rosary, etc.; weight, 11,000 Gm. (average for age, 15,700 Gm.)." Cod liver oil and a well balanced diet were prescribed and, in addition, calcium lactate was given. There is no means of knowing how well the treatment was followed, but the record at the University Clinic supplies the information that one month later the child was able to stand, and that the weight had increased more than a kilogram.

The next record of the child is that made in our own dispensary when he was 7 years of age, at which time he weighed 12,500 Gm. and measured 91 cm.

(average weight and height for that age are 20,800 Gm. and 115 cm., respectively). The degree of rickets was extreme. In addition to the great enlargements of the wrists, knees and ankles, the legs were markedly bowed and the abdomen formed a pot belly. The x-ray pictures taken at this time showed rickets, obviously of long standing and accompanied by the most extreme osteoporosis, with no evidence of healing. The shafts were enormously thickened. The humerus showed the outward curvature above the insertion of the deltoid, and the lower end of the femur and the upper and lower ends of the tibia showed the backward bends so characteristic of rachitic deformities acquired during the sitting period. The ends of the shafts exhibited great cupping, and when the nuclei of ossification of the epiphyses could be seen, they were quite a distance away from the crater-like endings of the shaft. These changes are well illustrated in the x-ray pictures of the lower ends of the radius and ulna (fig. 5*A*). The calcium of the blood serum was 12.2 mg. per hundred cubic centimeters; the amount of inorganic phosphorus was not determined.

Fig. 6 (case 20).—Photographs taken before and after eight months' viosterol therapy; and before and shortly after osteotomy for the correction of the deformities of the legs. The gain in height was 8.5 cm.

The amount of milk in the diet, which had previously been a pint (473 cc.), was increased to a quart (946 cc.) daily, and a daily dose of 60 drops of viosterol was prescribed. On his return to the dispensary a month after the viosterol treatment had been initiated, the child seemed stronger and had begun to walk about considerably, whereas previously, instead of walking, he had been crawling and, if placed in an erect position, would soon fall. The x-ray pictures taken at this time showed definite evidence of healing, which consisted notably in an extension and intensification of the terminal cups of the shafts. After two and two-third months of viosterol treatment, the density of the bones in general had increased, but the changes at the lower ends of the radius and ulna had become most striking. The end of the shaft of the radius had extended to such an extent that it now embraced the nucleus of the epiphysis and formed a great bell-like enlargement (fig. 5*B*). The nucleus of the epiphysis of the lower end of the ulna had not become visible.

The rims of the lower ends of both bones appeared irregular and scalloped, and cast a uniform dense shadow. After four and a half months of treatment, the serum calcium was 9.1 mg. and the inorganic phosphorus 5.2 mg. per hundred cubic centimeters. After six and a half months, the calcification at the ends of the shafts seemed to be complete, but the curvatures of the shafts and the irregularities in the finer architecture were more conspicuous. Seven months after the beginning of viosterol therapy, osteotomy was performed to correct the deformities of the legs. The fractures healed rapidly with good formation of callus, and the deformities were successfully corrected. From this time the child began to walk normally, and gained rapidly in weight and height. The height had increased 8.5 cm. during the seven months of treatment (fig. 6). Several of the permanent teeth had erupted. The x-ray pictures taken eight and a half, nine and a half (fig. 5*C*) and twelve and a half months after viosterol treatment had been commenced showed steady progress toward normal. In the last film of the series the humerus, radius and ulna were shown to have assumed more slender proportions.

The case is of great interest because of the ready response to viosterol in a most advanced type of rickets in a child 7 years old. Considering the large dosage employed, the healing induced by viosterol appears to have been somewhat slow, but in view of the age of the child and the severity of the rickets, a more rapid cure was hardly to be expected.

The child has now taken 60 drops of viosterol daily for twelve and a half months. He seems to be in perfect health, and the calcium and inorganic phosphorus of the serum after eight months of therapy are 9.6 and 6 mg. per hundred cubic centimeters, respectively.

Case 22.—F. A., a white girl, 10 years of age, was born at full term, was breast fed for two months and was then bottle fed until she was 2 years of age. She did not walk until the age of 21 months. She had never taken cod liver oil prior to her first visit to the Harriet Lane Home Dispensary, when she was 4 years old. It was then noted that the ends of the long bones of the extremities and the costochondral junctions were enlarged and that the knees knocked. The height was 96.5 cm. (average for her age, 96.7 cm.). A diagnosis of "chronic rickets" was made, and cod liver oil was prescribed. The orthopedists pronounced the rickets "too active for operative interference."

The child was not seen again until six years later, when she was 10 years old. The complaint was then made that the child ate poorly, refused green vegetables and took little milk, but consumed much cake and candy. No cod liver oil had been given for the preceding two years, but the child had been "out in the sunshine all summer." Though the mother thought that the child had improved, the enlargements of the ends of the long bones of the arms and legs were far greater, and the knocking of the knees had considerably increased. Cod liver oil and a well balanced diet were again prescribed. For the ensuing nine weeks the child returned to the dispensary regularly and seemed to be cooperating in taking the diet and the cod liver oil; then she did not appear for five months, during which the cod liver oil treatment was almost entirely suspended. On her return she was at once admitted to the hospital, and careful physical and roentgenologic examinations were made and viosterol treatment was soon started. The height was now 114 cm. (average height for the age, 131.5 cm.); that is, dwarfing had commenced. The rachitic enlargements at the cartilage shaft junctions of the ribs and of the long bones of the extremities were extremely marked. The thorax and arms were not badly deformed, but the legs were greatly bent and knock knee was extreme. On roentgenologic examination the lower ends of the radius and ulna were found to

be the seat of extreme rickets (fig. 7 *A*). The shafts seemed to end in irregular craters, at the base of which there was marked fringing with much cross-trabeculation. The epiphyseal centers of ossification were separated from the craters by an interval large enough to indicate that a deep rachitic intermediate zone was interposed. Probably on histologic examination irregular deposits of lime salts would have been found scattered through the intermediate zone.

A week after the patient's admission a daily dosage of 21 drops of viosterol was begun, and after two weeks daily treatment with ultraviolet rays from the mercury vapor arc in quartz was also commenced (exposure, front and back, for periods of one minute at first gradually increasing to six minutes, at a distance of two feet). At this time special precautions were taken to exclude renal rickets. The urine was normal; the specific gravity, on one occasion at least, was as high as 1.180; the phenolsulphonphthalein excretion was 78 per cent in two hours, and the blood pressure was also normal. The x-ray films taken seven and eighteen days, respectively, after the beginning of viosterol treatment showed possibly the slightest improvement at the cartilage-shaft junction, but these changes were not definite.

Fig. 7 (case 22).—Well marked rickets in a white girl, aged 10 years. Twenty-one drops of viosterol were administered daily for forty-five days, and coincidentally irradiation with the mercury vapor arc in quartz. *A*, the bones of the wrists before the treatment with viosterol was begun, showing a chronic type of rickets in which the disease and healing go on side by side. *B*, the same bones after forty-five days of the combined treatment. The healing effect is most clearly visible in the radius. A deposition of lime salts has occurred in the periphery of the crater, which gives rise to a new line in the x-ray picture. *C*, the same bones a year after all treatment had been stopped. The rickets has lighted up again and is worse than it was before viosterol therapy was begun.

After fifteen days of viosterol therapy there was slight elevation of the inorganic phosphorus in the blood serum (from 2.6 and 2.3 to 3.2 mg. per hundred cubic centimeters), while the serum calcium was slightly diminished (from 10.2 and 9.7 to 9.6 mg. per hundred cubic centimeters). An x-ray picture of the bones taken forty-five days after the viosterol treatment was commenced showed slight but definite spotty shadows of fresh deposits of lime salts at the ends of the shafts (fig. 7 *B*).

After a stay of nine weeks in the hospital the child was discharged. During this time it is certain that she received 21 drops of viosterol daily, and a daily treatment with ultraviolet rays from the mercury arc vapor lamp for the first

forty-five days. Accurate knowledge concerning the treatment following her discharge is lacking. For the three months following discharge the patient came in once a week for the purpose of receiving a single twenty-minute treatment with the ultraviolet rays; and it seems probable that she was given viosterol during that time but altogether improbable that she received it regularly. An x-ray film of the extremities taken two months after her discharge from the hospital showed no change in the rachitic condition. One taken eight months following the discharge showed perhaps a slight decrease in the rickets. During all of this time the child remained for considerable periods outdoors in the sunlight. Nine months after discharge her general condition was excellent, and the rachitic condition had improved to such an extent, in the opinion of the orthopedic surgeons, that an osteoclasis was performed. The formation of callus was good, and the bones healed readily. A week after the operation the daily dosage of viosterol was increased to 50 drops, but after a short time, the child stopped taking it entirely. X-ray pictures taken when she was 12 years old, more than a year after she had stopped taking viosterol, showed that the rachitic process at the cartilage-shaft junction had perhaps become slightly intensified (fig. 7 *C*).

The case is of interest and importance because the daily administration of 21 drops of viosterol, supplemented by treatment with the ultraviolet rays from the mercury vapor arc lamp, produced only slight change in the rachitic condition. The case is disappointing because large doses of viosterol, which would have constituted a real test, were not employed, and it is thus impossible to say that the rickets in this case could or could not have been cured entirely by large doses of viosterol. Although a daily dosage of 21 drops of viosterol over a period of forty-five days, supplemented by ultraviolet irradiations, produced a definite effect, the effect was surprisingly slight and indicated the presence of a powerful intrinsic factor which might have rendered the case a difficult therapeutic problem even with large doses of viosterol. It is interesting that the rachitic bends were of the type seen in renal rickets or in the rickets which develops after infancy (late rickets in the strict sense) rather than of the type seen in the usual case of persistent infantile rickets. It is also interesting that the child was not discommoded by the disease. Though the bones of the legs bent under the weight they carried, so that bowing occurred, the child led an active life, taking gymnasium exercises, skipping rope and participating in other athletic activities.

COMMENT

In our series of 23 children suffering from prolonged severe rickets, 12 were between 1 year and 8 months and 3 years of age, 5 between 3 and 4 and 6 between 4 and 10. With the exception of the case of "celiac rickets," all of the cases are probably of the persistent or recurring infantile form of the disease. As already stated, no case of renal rickets was included. The fact that we were able to find only 6 cases of late rickets according to Schmorl's definition (rickets in children 4 or more years old) shows the rarity of the disease in older children.

Effectiveness of Viosterol.—With a single exception (case 22), viosterol effected complete healing in all of the children during the period of observation. In one exception (case 22) the dosage of viosterol was, relatively speaking, small (21 drops daily for a child

of 10 years), and the period of administration was only forty-five days, so that the test of viosterol was not a fair one.[12] However, even in this case the viosterol produced a slight but definite effect of healing, as evidenced in the x-ray film, and it is possible that with a larger dose of viosterol and treatment continued over a longer period of time complete healing might have been obtained. It is also possible that this patient would have benefited by the addition of phosphate to the diet, since the level of the inorganic phosphorus in the serum seemed to remain consistently low in spite of viosterol and irradiation therapy.

Dosage of Viosterol Employed.—In our earlier work we used small doses of viosterol of from 10 to 20 drops daily. As our experience enlarged, we perceived the variability in the response of rickets to antirachitic agents and the necessity of giving larger doses. Accordingly, if the rickets was especially severe, if on trial the condition proved obstinate to treatment with cod liver oil or small doses of viosterol or if some special indication to bring about more rapid healing existed, we prescribed 60 drops of viosterol daily without hesitation. In some cases of severe persistent rickets the administration of from 10 to 20 drops of viosterol daily brought about complete healing within a short time; in others such small doses proved to be inadequate or effected healing slowly. Sixty drops of viosterol given daily caused rapid healing of the rachitic process in 5 of the 8 cases in which this dosage was employed and somewhat slow healing in 3. If one is certain that the rickets is not of renal origin and if 60 drops of viosterol prove on trial to be inadequate, one should not hesitate to use larger doses. Jampolis and Londe,[9] in one of their patients, a child of 2 years, increased the dosage of viosterol for a short time to 600 drops daily. If 60 or more drops of viosterol are administered daily, the concentrations of calcium and inorganic phosphorus in the serum should be followed carefully in order to be certain that the dosage of the drug has not reached a dangerous level.

The variability in the response of rickets to viosterol is illustrated in case 6 (that of a colored boy, aged 3⅓ years). Whereas in most cases the rickets did not reappear after therapy was discontinued, in this case the rickets recurred five months after the administration of viosterol had been discontinued. Physicians are in the habit of thinking that usually after the second, and certainly after the third year, treatment with vitamin D can be discontinued for the reason that the rachitic tendency diminishes as growth slackens, and that by the age of 3 years, a period has been reached at which the child begins to lead an outdoor existence and to avail himself fully of the antirachitic energy furnished

12. As has been made clear in the protocol, we know that the viosterol was administered for forty-five days. After the forty-five day period it was probably administered irregularly, but exact knowledge is lacking.

by sunlight. Though it is doubtless true that in most instances it is safe to discontinue the administration of cod liver oil or of viosterol after the second year, this case illustrates that it is not always possible to do so, even after the third year, and that the physician must be prepared to modify his procedure according to the particular indications, always taking into consideration the accessory factors in the etiology of rickets, such as race, diet, living conditions, climate and geographic conditions.

Harmlessness of Viosterol When Given for Months in Doses of from 10 to 60 Drops.—In case 19 (that of a colored boy 3½ years old) 60 drops of viosterol was administered daily for thirteen months and in case 20 (that of a colored boy, aged 7) for twelve and one-half months. In other cases 60 drops of viosterol were given daily for from six to eight months. In none of the cases were any toxic effects noted. A glance at tables 2 and 3, in which the concentrations of calcium and inorganic phosphorus in the blood serum after treatment with viosterol alone are given, will show that the concentrations in these cases remained within safe limits. It seems probable that the child with rickets (renal rickets excepted) has a greater tolerance for viosterol than the nonrachitic child. Certainly, if the viosterol is not producing a marked antirachitic effect, which can be judged from the x-ray film, it should not cause toxic manifestations or metastatic calcification. The danger from overdosage with viosterol in the child with rickets occurs probably only after the viosterol has brought the rachitic state to an end. All that we actually know, however, from our series of cases is that in none of them did viosterol produce a disturbance in the health or well-being, though it was given to some children in large doses for long periods of time. We also had the opportunity of studying the tissues of several children who died of diseases not associated with viosterol therapy, but who were receiving viosterol in doses ranging from 10 to 60 drops daily for long periods, and in none of these was evidence of toxicity found grossly or histologically.

Race Incidence.—It is interesting that all but 2 of the 23 children of the series were colored and that 1 of the 2 white children had rickets combined with celiac disease. In their investigation of rickets in New Haven, Conn., Eliot and Souther [4] found not only that the percentage incidence of mild rickets was much greater among the colored than among the white children, but that the incidence of the severe protracted forms of the disease was also greater among the colored children. Although, on a priori grounds, a great preponderance of colored over white children was expected in our group, the 21 : 2 ratio of colored to white children was surprising. In the Harriet Lane Dispensary, through which all patients, including those of the hospital and special clinics, pass, the numbers of colored and of white children regis-

tered are approximately equal. Tuberculosis is thought to be much commoner in the colored than in the white race, yet in our clinic for tuberculosis the numbers of colored and white children admitted are approximately the same. Therefore, the large number of colored children, as compared with white children in our series of cases of rickets, is a striking illustration of the prevalence of rickets in severe form in the colored race. The greater incidence is probably due to the fact that the diet and the living conditions of the colored children in Baltimore are, on the average, far inferior to those of the whites, and the Negro mother in Baltimore is, on the whole, much more indifferent and unobservant of the health of her children than is the white mother. In consequence, she is less liable to seek medical aid early and is less persistent and reliable in carrying out medical treatment even when it has been made available. Possibly the dark skin and an inherited racial susceptibility are additional factors in causing the high incidence of rickets in the colored child.

Persistence of Rickets.—Since 21 of the 23 children were colored, the persistence of severe rickets in our series is to be attributed, essentially, to the combination of factors just recorded. The diets of most of the Negro children in Baltimore are composed chiefly of carbohydrates in the form of bread, syrups and jams, cake and candy and contain but little milk, while breast feeding is often continued into the second year. The diets of some of our patients were known to be defective. In cases 8, 15, 19 and 20, milk, which is the only abundant source of calcium and phosphorus in the diet, was entirely lacking, and in case 19 a dietary deficiency was suspected because of the low concentration of the serum calcium and the slow healing during treatment with viosterol. The rickets in these Negro children is thus etiologically analogous to that produced by Mellanby [13] in puppies by feeding diets composed of white bread and small quantities of milk, the ultraviolet ray factor having been excluded.

In cases 8 and 23, in addition to the defective diet, mental retardation was an indirect cause of the persistence of the severe rickets. Because of the mental defect the children could not care for themselves outdoors, and so were kept in the house except after the parents returned from work in the evening. Late rickets is far more common in mentally defective than in normal children, not only because they are neglected, but also because they are apt to be fed diets suitable for the infant rather than for the older child; it is common to find mentally defective children 3 and 4 years old fed little else than milk and cereals.

In another of our patients (case 18) the rickets developed during a succession of illnesses. These illnesses may have been contributory

13. Mellanby, E.: Experimental Rickets, Medical Research Council Special Report Series no. 61, London, His Majesty's Stationery Office, 1921.

factors. Chronic infections of the respiratory tract, in particular, seem to favor the development of rickets. This relationship may be due to a direct disturbance in the mechanism governing the calcium and phosphorus equilibrium in the body or to the indoor confinement and the suspension of antirachitic agents during such illnesses.

Finally, in 1 of our patients celiac disease seems to have been contributory to the development of rickets.

In general, the older the patient with rickets, the more obvious is the reason for the existence of the disease, and in the majority of cases of late rickets one can discover defects in diet or hygiene. In the infant, on the other hand, it is more common not to find an explanation for the existence of the disease. In the older child in whose case a dietary or hygienic deficiency cannot be found, intrinsic as well as extrinsic causes may be responsible for the development of rickets. This intrinsic tendency varies greatly in children, and the exact cause of such a tendency is not well understood. In case 22, that of a white girl, aged 10, the intrinsic factor must have been the essential one, and in case 19, that of a colored boy, aged 3 years, it is reasonably certain that the cause was in part intrinsic from the fact that the rickets responded so slowly to treatment with viosterol, even after the diet was made adequate. In case 6, that of a colored boy, 3⅓ years old, five months after the treatment with viosterol had been discontinued the discovery was made that the rickets had recurred. Although the presumption is that following the complete healing achieved with viosterol the boy was subjected again to the conditions under which the rickets had developed, nevertheless, the mere fact that the disorder reasserted itself after the age of 4 makes the existence of an intrinsic factor seem highly probable. In such children, in whom the rachitic tendency is too powerful to be overcome by the administration of cod liver oil, ultraviolet irradiation or small doses of viosterol, larger doses of viosterol may effect rapid healing.

Length of Time Required for Healing under Treatment with Viosterol.—Practically speaking, one cannot tell in the living child exactly when rickets has healed. Since rickets depends on a disturbance in the calcium-phosphorus metabolism with the result that lime salts are not deposited in the growing parts of the skeleton, the disease is healed at the moment when this abnormal state is fully corrected. Perhaps, if the determinations of the concentrations of calcium and inorganic phosphorus in the blood could be repeated often enough or studies of the calcium-phosphorus balance made, one could date accurately the end of the rickets. Ordinarily, one is forced to rely on x-ray films. But the films, at best, even though taken in series, enable one to recognize in only the roughest way three stages in the healing process: (1) when the lime salts begin to be deposited freely at the cartilage-shaft junctions; (2) when the end of the shaft, including the rachitic

area, has become so heavily impregnated with lime salts that it stands out clearly and (3) when the ends of the bones have assumed an approximately normal definition and appearance. In the average case of infantile rickets with the patient under treatment with 3 teaspoonfuls of potent cod liver oil daily, the deposition of lime salts at the cartilage-shaft junctions appears within about twenty-one days; the ends of the shafts seem to become fully impregnated with lime salts at about the end of two months, and the ends of the bones approximate a normal definition and appearance after about five months. It is most important to appreciate, however, that these time criteria are not only most indefinite but are subject to the greatest possible variation, and that they depend both on the dosage of vitamin D employed and on the extent of the rachitic process at the cartilage-shaft junctions. For example, if large doses of viosterol are employed, deposits of lime salts may appear at the cartilage-shaft junctions in as short a time as a week or ten days; if the rickets has been of short duration, so that the rachitic zones at the ends of the shaft are narrow, the ends of the shafts will be completely impregnated with lime salts and will present an approximately normal appearance in the x-ray film in a much shorter time than if the rickets has been of long duration and has caused the formation of deep zones of uncalcified cartilage and osteoid at the ends of the shaft. Moreover, in gaging the time required for healing by means of the x-ray film a further difficulty arises in that the films are ordinarily not taken often enough or at sufficiently regular intervals to catch the healing process at exactly the right stage of development. For example, in case 14, stage 3 had not been quite reached three months after viosterol therapy was begun, but had been fully reached when the next x-ray film was taken six months afterward. Obviously, stage 3 occurred somewhere between the third and ninth months. For all these reasons we are unable to give more than impressions concerning the length of time that was required for healing by means of viosterol in our cases. Indeed, we can say merely that in some of our cases small doses of viosterol as well as large doses effected healing with great rapidity, but that in other cases the process of healing induced even by large dosage was slow. Doubtless, in every case rapid healing could have been attained if a dosage of viosterol had been chosen which was large enough to overwhelm the disease at the outset.

Viosterol as Compared with Cod Liver Oil.—As emphasized by the experience of Eliot,[4] it is easy to prescribe cod liver oil, but in the case of the average patient in the dispensary it is difficult to ascertain whether it has been taken regularly. Our social workers find that the administration of cod liver oil continues for a short time and then lapses. Viosterol, however, is given with much more regularity.

Cod liver oil was ordered in the majority of the cases in our series, but in most of them it was given irregularly, if at all. In only 3 cases

do we know that the cod liver oil was taken conscientiously in the period preceding viosterol therapy. Though in all these cases (1, 9 and 18) the x-ray films taken just prior to the treatment with viosterol showed that cod liver oil had produced an effect of healing, they also showed that it had failed to bring about complete healing.

Writers on rickets who report failures obtained with cod liver oil therapy but subsequent healing obtained by means of viosterol lead the reader to infer, perhaps, that the two substances are therapeutically different. In reality, with the exception of vitamin A and the food value of the oil, cod liver oil and viosterol represent merely different concentrations of the same vitamin. Cod liver oil and equivalent small amounts of viosterol produce an effect in rickets, but the effect may be so small as not to be demonstrable by the ordinary methods of examination. To understand the relationship of cod liver oil and viosterol, when considered as antirachitic agents, one must grasp two facts: First, there are all degrees of rickets, for example, florid rickets with no deposition of lime salt at the rapidly growing ends of the long bones and rickets with 10, 30, 50 or 98 per cent of the normal deposition of lime salts, as the case may be. Second, rickets may continue in the same state of activity for weeks, months or years. When the rachitic tendency is especially powerful, either from extrinsic or from intrinsic causes or from both, a relatively weak antirachitic agent like cod liver oil merely raises the healing process in the newly forming bone and cartilage to a somewhat higher level. Cases 18 and 19 afford examples. In case 18, cod liver oil given in large doses over a period of three and a half years had checked the rickets at a stage of partial development, but had been unable to cure it. When 40 and later 60 drops of viosterol were given, the rickets was brought to an end in a short time. In case 19, the administration of 20 drops of viosterol daily caused a sharp reaction of healing within eighteen days, but did not entirely check the rickets, which remained in the same state of partial healing for the ensuing eight months. When, however, the dosage of viosterol was increased to 60 drops it effected a complete cure in five months. Thus, the great value of viosterol lies in its concentration in the D factor, and, to a lesser extent, in its ease of administration, and therefore it is capable of preventing and curing rickets when other antirachitic agents prove inadequate.

Additions of Calcium and Phosphorus to the Diet in the Treatment of Rickets.—It seems possible that the failure of late rickets to respond to antirachitic treatment may occasionally be partly due to the overzealous addition of calcium salts to the diet, as in case 20. The reasons for making the suggestion are founded chiefly on the results of experiments with the rat. Indeed, in this animal, if the dietary phosphorus is low, the rickets-producing properties of the diet are greatly enhanced

by increasing the calcium. In experiments with low phosphorus rickets, the antirachitic effect of vitamin D can be increased by decreasing the calcium or, far better, by increasing the phosphorus intake. Conversely, the antirachitic activity may be diminished by decreasing the phosphorus or increasing the calcium intake. Thus, if late rickets of the low phosphorus type is to be maximally benefited by vitamin D, the phosphorus intake must be adequate and the calcium intake must not be increased out of proportion to the phosphorus level. The phosphorus of the diet may readily be increased by incorporating phosphorus-containing foods, such as meats, or inorganic phosphate. In a few cases of severe infantile rickets, rapid healing has been brought about by means of the administration of viosterol and the addition to the diet of 3 Gm. of disodium acid phosphate (anhydrous) daily for short alternating periods.

Value of Effecting Rapid Healing of Rickets.—The value of bringing the rickets abruptly to an end is well illustrated in case 19. Manual osteoclasis was performed on the patient when he was 3¼ years old and while the rickets was still active. Although the straightening of the legs was accomplished by means of the operation, the condition shortly afterward became worse than it had ever been, because the legs bent again as soon as the child began to walk. If adequate amounts of viosterol had been administered immediately after the operation, as was done in cases 11, 15, 20 and 21, the legs would have acquired within a few weeks sufficient rigidity to support the weight of the body without yielding. The value of effecting rapid healing in rickets is also of importance in cases of severe "thoracic rickets," described by Park and Howland.[14] These authors have found that in children under 2 years of age suffering from the combination of rickets and extreme malnutrition, the thorax is often weakened and lacks rigidity, so that it fails in its function as a bellows. Most of the childen with this condition have respiratory infections, but the infections themselves are relatively mild; it is in the loss of rigidity of the thorax that the essential danger lies, predisposing them as it does to atelectasis and pneumonia. For this reason it is essential to change the thorax from a collapsing into a rigid bellows with the least possible delay, and by far the best means of accomplishing this is the giving of viosterol in large doses.

Slumbering Character of Rickets in the Older Child.—An interesting feature of case 22 was the slight extent to which the disease interfered with the activity and well being of the patient. This 10 year old girl took part in athletic exercises at school and skipped rope and was made conscious of the disease only through her visible deformities. In the

14. Park, E. A., and Howland, J.: The Dangers to Life of Severe Involvement of the Thorax in Rickets, Bull. Johns Hopkins Hosp. **32**:100, 1921.

case of the rachitic dwarf the disease probably continues for years, but ceases to give rise to any conscious disturbance as the child grows older. Both the patient and the physician therefore assume that all activity is long since past, whereas the disease continues to smolder.

Celiac Rickets.—The osteoporosis and rickets in the patient with celiac disease were completely cured by the diet and by the daily administration of 40 drops of viosterol within four months, as contrasted with the nine months which was the average period of cure for Parsons'[15] patients, who were treated with ultraviolet irradiation or with irradiated *dry* cholesterol. Aside from the diet aimed specifically to alleviate the intestinal derangement in celiac disease, provision should be made for an adequate intake of calcium. The diets high in protein and low in residue prescribed in celiac disease are usually high in phosphorus. On such diets with a relatively inadequate supply of calcium, the attempt at calcification by means of antirachitic agents may lead to tetany. This is especially likely to occur when the stools are still fatty and contain much calcium. The constant excretion of calcium in the stools and its diversion to the bones for calcification robs the blood of its available calcium, and tetany may thus ensue.

Viosterol and Renal Rickets.—A word of caution seems appropriate in regard to the use of vitamin D in another form of late rickets, namely, renal rickets. Patients with this condition usually have retention of phosphorus and are unable to excrete it in the urine. The excretion of phosphorus as the insoluble calcium salt by way of the feces results in the high phosphorus-low calcium type of rickets. In such cases, the constant transport of calcium phosphate in the blood in excess of its solubility may lead to metastatic calcification in the soft tissues, especially in the medial coats of the medium-sized arteries. Since vitamin D not only increases the calcium but also the inorganic phosphorus in the serum, the injudicious use of vitamin D preparations may enhance the occurrence of abnormal calcification. Shelling[16] and Shelling and Asher[17] showed that animals retaining excess amounts of phosphorus, either through the feeding of diets high in phosphorus or as a result of parathyroidectomy, are more susceptible to abnormal calcification and to the toxic effects of viosterol than are normal animals, and Karelitz

15. Parsons, L.: The Bone Changes Occurring in Renal and Coeliac Infantilism and Their Relationship to Rickets: II. Coeliac Rickets, Arch. Dis. Childhood **2**:1 (Feb.) 1927; Celiac Disease, Am. J. Dis. Child. **43**:1293 (May) 1932.

16. Shelling, D. H.: Rôle of Parathyroids in Calcification and the Susceptibility of Parathyroidectomized Rats to Viosterol, Proc. Soc. Exper. Biol. & Med. **28**:307, 1930.

17. Shelling, D. H., and Asher, D. E.: Calcium and Phosphorus Studies: IV. The Relation of Calcium and Phosphorus of the Diet to the Toxicity of Viosterol, Bull. Johns Hopkins Hosp. **50**:318, 1932.

and Kolomoyzeff [18] recently reported roentgenologic evidence of arterial calcification in a patient with renal rickets treated with viosterol For this reason, it would seem logical that in this type of rickets, diets high in calcium and, relatively speaking, low in phosphorus should be used, and that vitamin D should be employed cautiously or not at all.

SUMMARY

1. Twenty-two of 23 patients with late rickets treated with viosterol were cured completely. The one exception was a 10 year old girl who was treated with a moderate daily dose of viosterol for only forty-five days.

2. The greater prevalence of rickets among colored children is evident from the fact that, in our series, 21 were colored and only 2 were white. In 1 of the white children the rickets was a complication of celiac disease.

3. Some of the children received usual amounts of vitamin D before viosterol therapy, while others had not received previous therapy. The usual amounts of vitamin D, even when administered over a long period of time, produced only partial healing, but when larger amounts of viosterol were administered healing occurred fairly rapidly and completely.

4. In none of the patients treated with fairly large doses of viosterol was clinical evidence of toxicity noted, even when the therapy was continued for more than a year.

5. In 7 of the patients osteotomy or manual osteoclasis was performed for the correction of rachitic deformities before or during viosterol therapy. Complete union at the site of operation occurred in all cases. The corrective results, however, were much better in the cases in which rapid healing was induced by larger doses of viosterol, since the rigidity which the legs thus acquired enabled them to withstand the weight of the body without yielding.

6. The factors which enhance or hinder the activity of viosterol in late rickets are enumerated and discussed.

7. Attention is called to the inadvisability of using vitamin D preparations in renal rickets.

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18. Karelitz, S., and Kolomoyzeff, H.: Renal Dwarfism and Rickets, Am. J. Dis. Child. **44**:542 (Sept.) 1932.

Case Reports

COARCTATION OF AORTA—ULCERATIVE AORTITIS —PERFORATION OF AORTA AND ACUTE PERICARDITIS

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Coarctation, or stenosis of the aorta in the region of the ductus arteriosus, has been divided into two types.

The infantile type consists of a narrowing of the aorta between the origin of the left subclavian artery and the site of the ductus arteriosus. It is an exaggeration or persistence of the anatomic condition found in the fetus.

The adult type has no counterpart in normal intra-uterine life. It consists of a sharp constriction, at times complete obliteration, of the aorta, adjacent to the insertion of the ductus arteriosus. In this type, the symptoms of the condition may go unnoticed until some intercurrent infection weakens the myocardium, or until some exertion increases the hypertension in the dilated vascular tree in the upper part of the body beyond the vascular reserve. Persons with such a condition may not complain of symptoms until the ages from 20 to 40. The condition has been found in a 92 year old man.

In a study of two hundred cases of coarctation in persons above 2 years of age, Abbott[1] found the great majority to be of the adult type. The degree of stenosis of the aorta is described as being complete in forty-seven, extreme in one hundred and eight and moderate in forty-five; in others the degree was not mentioned. The ductus is usually closed.

Coarctation is usually associated with other congenital anomalies; graver and more complicated ones are seen in the infantile type and practically never in the extreme degrees of the adult type, in which,

From the Research Hospital.
Read before the Central States Pediatric Society, Oct. 7, 1932.

1. Abbott, M. E.: Coarctation of the Aorta of the Adult Type. A Statistical Study and Historical Retrospect of 200 Recorded Cases, with Autopsy, of Stenosis or Obliteration of the Descending Arch in Subjects Above the Age of Two Years, Am. Heart J. **3**:381, 1928.

however, minor abnormalities are relatively frequent. Of the two sexes, the male is by far the more commonly affected.

Spontaneous rupture of the aorta occurred in forty cases; twenty-four patients died of cerebral lesions, commonly hemorrhage; sixty died of decompensation, and seventeen died suddenly, without apparent cause.

There were fourteen cases of endarteritis; of these thirteen were at the site of the coarctation and of these three had ruptured. In the fourteenth case a mycotic aneurysm was in the ascending aorta, and rupture had occurred into the pericardium. The frequency of an

Fig. 1.—Photograph showing normal aortic valves, absence of atheromatous plaques, coarctation and two ulcerated areas above the aortic valve.

infective lesion at the site of coarctation is attributed to the dilatation and atheroma of the aorta proximal to the stenosis, and to kinking and deformity, which provide a favorable nidus for the lodgment of bacteria.

In the cases of rupture following arteritis the patients were two boys, aged 10 and 17, and a girl, aged 12. Streptococcus viridans was the organism in two of the cases and pneumococcus in one. Poynton and Sheldon [2] reported a case of coarctation with ulcerative aortitis due to Streptococcus haemolyticus, without rupture, in a boy aged 8 years.

2. Poynton, F. J., and Sheldon, W. P. H.: Coarctation of the Aorta with Ulcerative Aortitis, Arch. Dis. Childhood **3**:191, 1928.

REPORT OF A CASE

History.—B. B., aged 7, was admitted to the Research Hospital, service of Dr. Harry Gilkey on Feb. 23, 1931. He was born normally at full term, and was breast fed. He had chickenpox at the age of 2 years. In May, 1930, he had been given tetanus antitoxin, following which pains in the joints developed with swelling, which lasted two weeks. In August, 1930, there was another attack of pains in the joints lasting a few days. The tonsils were removed in September, 1930. Early in February, 1931, otitis media developed, with rupture of the drum and discharge of pus; following this the pains in the joints recurred and persisted until the time of admission. The pain and swelling of the joints were migratory.

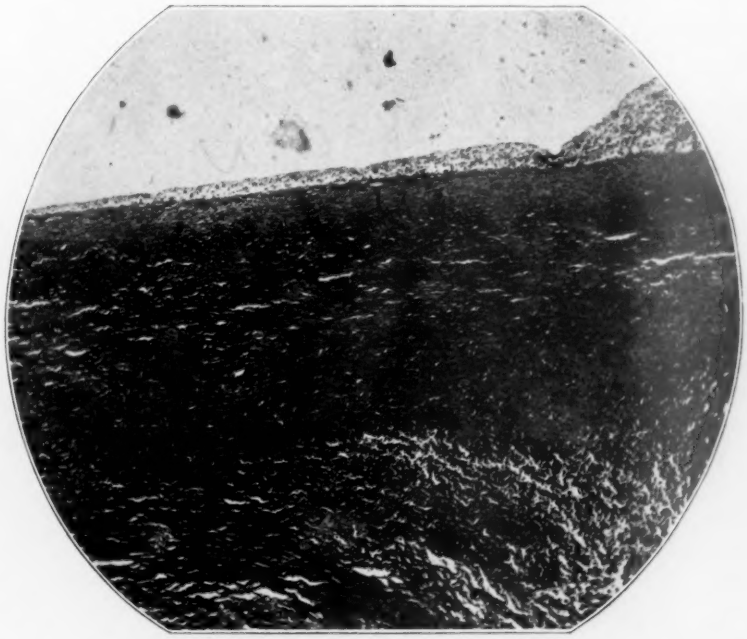

Fig. 2.—Low power photomicrograph showing the inflammatory exudate on the intima, the exudate increasing in thickness on approaching the site of ulceration.

Dyspnea was noticed for two weeks and a nonproductive cough for four days before admission.

Examination.—The patient was about normal in development and weight for his age. He was pale and dyspneic. The respiratory rate was 40; the temperature, 100 F., and the pulse rate, 100. There was a slight bilateral cervical adenopathy. The ears were negative for inflammation or perforation. The chest was barrel-shaped; the left side of the chest was larger than the right, and the respiration was labored. The apex impulse of the heart was in the anterior axilliary line. The left border of the heart was in the midaxillary line and the right border 2.5 cm. from the right sternal margin. The muscle sounds were of poor quality; there was a systolic murmur at the apex. The lungs were normal on percussion; râles (dry) were heard throughout both lungs. The abdomen was slightly distended; there was slight tenderness, generalized, with no masses. The extremities showed no edema, redness or swelling of the joints. Urinalysis gave negative results.

Examination of the blood showed: hemoglobin, 55 per cent; red cells, 3,450,000; and white cells, 30,000, with polymorphonuclears 71 per cent. On the basis of roentgenograms of the chest a diagnosis of pericardial effusion was made.

The patient died on February 26.

Autopsy.—The pericardial sac contained a large amount of fluid and clotted blood. The pericardial surfaces were covered with a thick, inflammatory exudate. The heart weighed less than 200 Gm. The myocardium was not thickened and

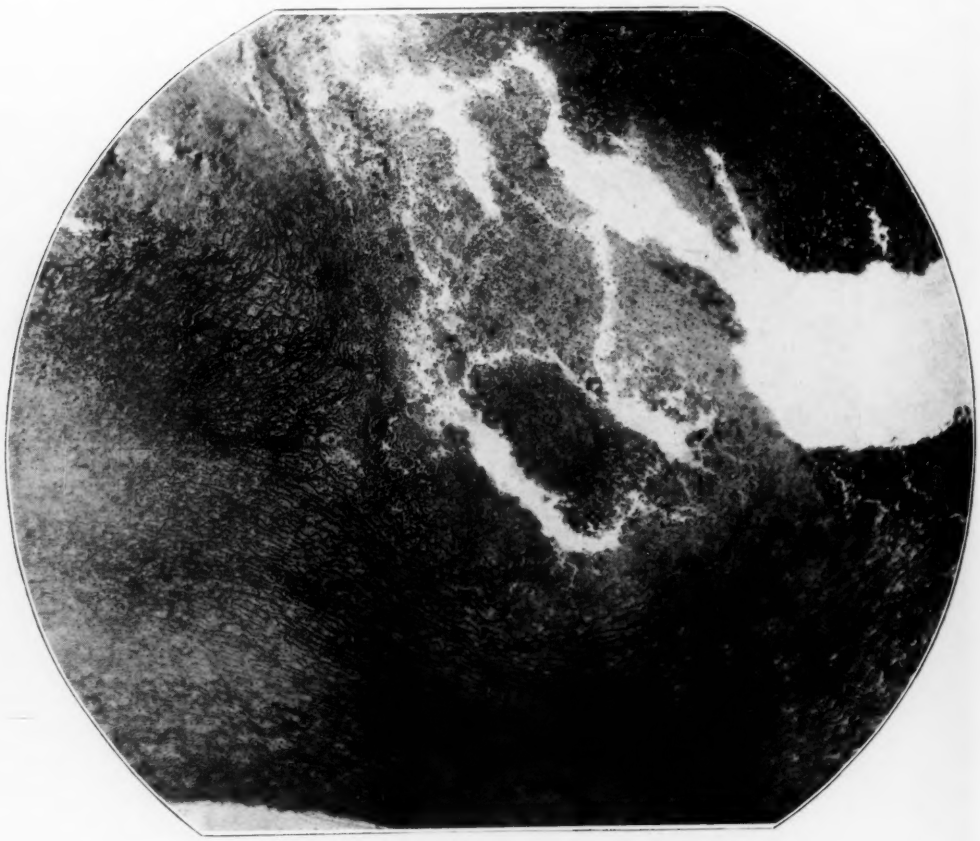

Fig. 3.—Photomicrograph of the suppurative process, showing the division of the elastic fibers to swing above and below the abscess.

was slightly flabby. The foramen ovale was closed; the valves were not abnormal; the coronary ostia were normal, and the arrangement of the vessels of the aorta was normal. The aorta at the base measured 4.5 cm. in circumference. About 5 cm. from the base, the aorta became narrowed abruptly; at the junction of the aorta and the ductus arteriosus, which was closed, the narrowing of the aorta was moderate. In the left mesial side of the aorta, about 3 cm. above the base, there was an irregular, rentlike opening, partially filled with a dark red blood clot. At the edges of the opening there were two vegetations, the larger one measuring 5 mm. in diameter and the rent measuring 8 mm. in length. A second punched-out

lesion, 1 mm. in diameter, was situated 3 mm. posterior to the first ulcer; this opening communicated with a dissecting aneurysm, which was 2 cm. in its greatest length, and with the pericardial sac.

Microscopic examination of the aorta at the site of the perforation showed a polymorphonuclear exudate (abscess) in the media with the elastic fibers dividing to run below and above the inflamed area. The abscess communicated with the lumen of the aorta, on the intimal surface of which there was an exudate consisting of fibrin with an occasional polymorphonuclear leukocyte.

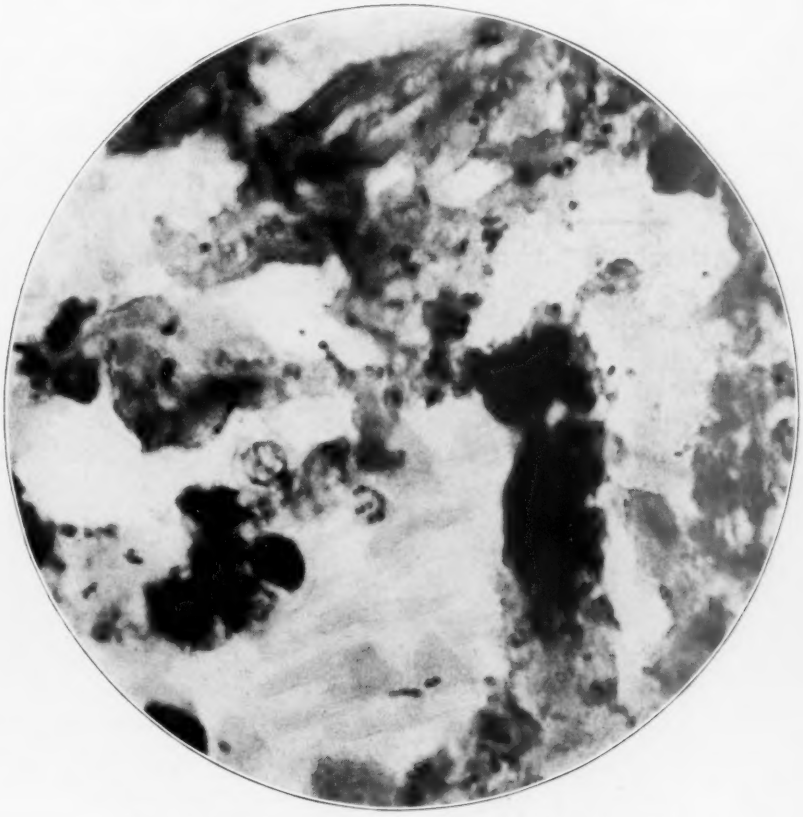

Fig. 4.—Streptococci in the exudate within the aorta.

Bacterial stains on sections of the inflamed aorta showed streptococci in the polymorphonuclear exudate.

A culture of the blood made post mortem showed Streptococcus infrequens (hemolytic).

COMMENT

Coarctation of the aorta is a comparatively rare congenital anomaly. In a small number of such cases endarteritis has been reported, occurring just above or below the site of coarctation. This site is considered a locus minoris resistentiae. No doubt atheromatous plaques and

ulcers, which commonly occur proximal to the stenotic area, favor surface infection, dissecting aneurysms and rupture. In the case under consideration there were no atheromatous ulcerations or plaques to give support to the theory of surface invasion of bacteria. The size of the suppurative process in the media of the aorta and the division of the fibers of the media of the aorta to swing above and below what we believe was the primary lesion suggest that the infective agent reached the site through the vasa vasorum, and that the primary lesion was therefore an acute infective mesaortitis, with the production of an abscess of the aortic wall. As the abscess increased in size and approached the aortic lumen, an inflammatory exudate was produced on the aortic intima, eventually ulcerating through the intima. The extension of the inflammatory process toward and through the adventitia produced the pericarditis, there being a direct communication to a probe between the aortic lumen and the pericardial sac. It also appears to us that the outward and inward inflammatory process in the aorta continued simultaneously, and that the pericardium had been infected for a considerable period, judging from the thickness and the extent of the pericardial exudate, which in one area measured 1 cm. in thickness, and the fact that the pericardium and epicardium were generally involved.

Unfortunately, during the attack of acute otitis no smears or cultures were made from the purulent discharge. It seems likely that the otitis media was the focus from which bacteria reached the aorta. The infection of the ear occurred about three and one half weeks before death and only one week before dyspnea developed.

SUMMARY

A case of coarctation of moderate degree complicated by acute aortitis produced by Streptococcus infrequens, which proceeded to ulceration of the aorta, dissecting aneurysm, perforation of the aorta and acute pericarditis in a boy, aged 7 years, is presented.

NEOPLASM OF THE CHOROID PLEXUS

REPORT OF A CASE WITH REVIEW OF THE LITERATURE

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Neoplasms of the brain in infancy undoubtedly occur with greater frequency than reports of their discovery would suggest. Because of the readiness with which their symptomatology may be confused with that of gastro-intestinal dysfunction, particularly projectile vomiting, uncomplicated by a lesion of the nervous system, recognition of the presence of such tumors is incumbent on the pediatrician.

To the following case presentation have been appended citations of the literature dealing with the type of tumor described.

REPORT OF CASE

History.—C. E., a boy of 9 months, born of American parents, was admitted to Seaside Hospital of St. John's Guild on Aug. 6, 1931.

The parental history was irrelevant, and the birth of the infant, which followed about a year after that of a normal child, was noninstrumental and of short duration. The birth weight was 6¼ pounds (2,840.9 Gm.). The early postnatal history was uneventful and uncharacterized by the occurrence of convulsions, hemorrhage or jaundice.

The patient was nursed for two months and thereafter did well during the remainder of the first six months of life on modified whole milk supplemented daily by orange juice.

Beginning soon after the age of 8 months, and for at least two weeks before admission to the hospital, vomiting, although not projectile, had been frequent, characterized by the presence of mucus, and at times observed after every feeding. Constipation also had been obstinate, and for four days before the case came under observation there had been no stool. Following the development of the vomiting, boiled skim milk, lactic acid milk and, finally, thick cereal gruel without milk and sugar had been attempted without definite improvement. Notwithstanding a reported weight of 17½ pounds (7,937.8 Gm.) seven weeks earlier, the infant's weight on admission was only 14½ pounds (6,577 Gm.).

Clinical Findings and Course.—On physical examination, the baby appeared fairly well developed but chronically ill, asthenic, listless and moderately dehydrated. Congested tonsils, erupting lower incisors and undescended testes were

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From the Department of Pediatrics of New York University and the Children's Medical Service of Bellevue Hospital. Case record from Seaside Hospital.

noted. The circumference of the head was 17¼ inches (43.19 cm.), and the anterior fontanel, measuring about ¾ inch (1.87 cm.) was slightly depressed. No signs referable to the central nervous system were at first apparent, and there were no abdominal signs suggestive of pyloric spasm or obstruction. The temperature, 99.5 F. on admission, remained between 98 and 100 F. during the six days from admission to termination of the case. Urinalysis, nose and throat cultures and an intradermal tuberculin test gave negative results. Gastric lavage returned clear, but roentgenologic examination following a barium meal given two days after admission showed almost complete retention of the barium after six hours despite the normal roentgenologic appearance of the stomach in size, shape and position. These roentgen findings seemed indicative of pylorospasm.

For six days from the time of admission to the hospital, while the infant was being fed on a mixture of thick farina made up with skim milk and dextrimaltose,

Fig. 1.—Gross specimen, showing tumor of choroid plexus in left lateral ventricle.

he continued to vomit from one to four times daily, at the same time maintaining fair intestinal digestion as shown by normal stools. Body weight was well maintained by intraperitoneal injections of Hartman's solution and of saline, but the general condition became steadily worse and, gradually, significant neurologic manifestations were added to the apathy and stuporous appearance.

The following points were noted: inconstant deviation of the eyes to the left and upward, inconstant horizontal nystagmus, sluggish pupillary reactions to light and in accommodation, doubtful ability to follow a light with the eyes, definite papilledema of the right eye with beginning papilledema of the left and definite right facial weakness.

A spinal tap on the day following admission yielded 1 cc. of slightly "smoky," xanthochromic fluid under no increased pressure, containing many red corpuscles, forming no pellicle on standing and bacteriologically negative. A subsequent spinal tap gave identical findings without an increase in white cells. Subdural taps were negative.

In order to confirm more positively the belief that the patient had a tumor of the brain, ventricular punctures were performed at this stage. The taps of both ventricles yielded xanthochromic fluid under greatly increased pressure, to the amount of 25 cc. from the right ventricle and 70 cc. from the left. Following these

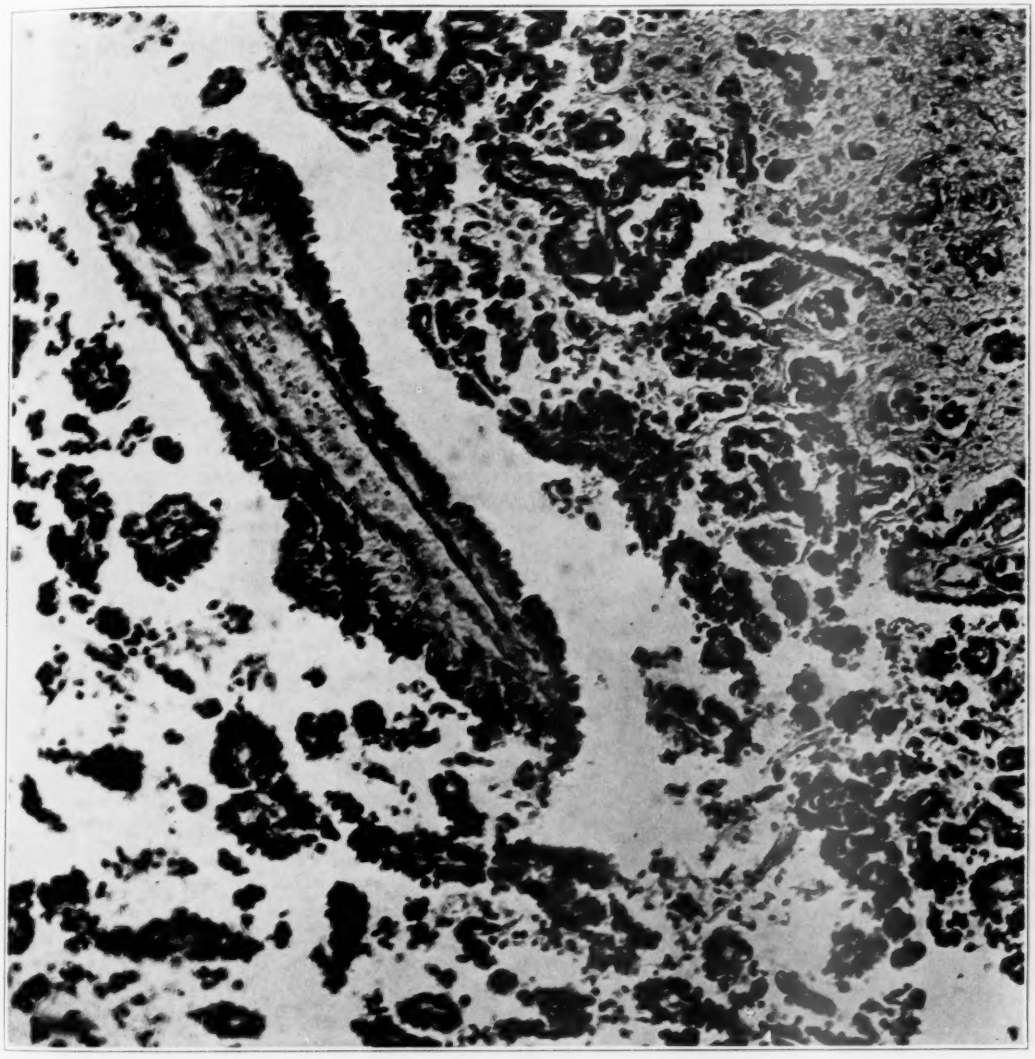

Fig. 2.—Microscopic section of tumor shown in figure 1.

taps the fontanel was markedly depressed, and a positive Macewen's sign was noted.

In spite of attempts to remedy dehydration the child became steadily worse and died suddenly six days after being admitted to the hospital and from four to six weeks from the time the digestive disturbance took on a serious aspect.

Autopsy.—Postmortem examination was made by Dr. Albert Byrne, and the histologic examination was completed by Dr. A. S. Price. (The negative autopsy observations are here omitted.)

The body was well developed but emaciated; the head was well shaped. With the exception of the evidences presented by the lungs, stomach and brain, the findings were not significant. The left portions of both lobes of the left lung showed static congestion. The stomach, although much distended, was found normal, with a normal pylorus.

Other findings confirmed the diagnosis of neoplasm of the brain. "In the posterior portion of the left lateral ventricle is a soft encapsulated tumor about 3 cm. in diameter, protruding from the lateral wall of the ventricle into the ventricle. On the anterior aspect of the tumor is a blood clot about 2 cm. in diameter indicating a recent hemorrhage. The clot is unorganized."

Histologic Report.—"The specimen consists of both hemispheres of the brain separated in the midline. To the base of the right half is attached a thick-walled sac, apparently made up of the falx cerebri, tentorium, and dura. The lateral ventricle on this side is dilated. The fourth ventricle is also somewhat dilated. There is no evidence of tumor growth in this part of the brain.

"On the left side there is some dilatation of the lateral ventricle particularly in the posterior portion. In the posterior portion of the lateral ventricle is found a large, friable, tumor mass which on the surface has a somewhat ragged, moth-eaten appearance. It forms a tumor somewhat irregular in outline, but measuring about 3 cm. in diameter. It has an appearance suggesting that it may have arisen in part from the choroid plexus. It peels away from the brain substance at its anterior margins and remains fixed only in the middle and lateral portions. It seems to have its origin in the posterior portion of the parietal lobe, just in front of and lateral to the occipital lobe. On removal, it leaves a triangular cavity, measuring 5 cm. at the base, 4 cm. anteriorly, 7 cm. superiorly, and about 2.5 cm. in depth. Several small blood clots are found.

"Microscopical examination shows a moderately anaplastic, hyperchromatic, epithelial growth which is somewhat papillary in type. Its origin seems to be fairly definite, and from the choroid plexus.

"Diagnosis: Papillary carcinoma of the choroid plexus."

Supplementary Note: "Microscopically the tumor is of a low grade character. It might be better, in the absence of metastases, to call the tumor papilloma although it is usually classified among the carcinomata."

COMMENT

Incidence of Tumors of the Choroid Plexus.—Although a considerable review of the literature antedating the case here reported has failed to reveal the occurrence of a neoplasm of the choroid plexus in any other subject so young, a strikingly similar instance was reported by Butterfield [1] coincidentally with the development of our case. His subject was only 3 months old when symptoms became significant. Vomiting had been frequent during the early weeks, and a fortnight before the patient was hospitalized, left internal squint, enlargement of the head with prominent veins and bulging fontanel were noted. Subse-

1. Butterfield, D. L.: Brain Tumors, New York State J. Med. **32**:1007 (Aug. 15) 1931; case 12.

quently a verified papilloma of the choroid plexus was successfully excised. As a result, the cerebrospinal fluid block that had existed was relieved, and eight months after operation this infant, although seriously handicapped by a persistent partial right homonymous hemianopia, petit mal seizures and retarded mental growth, nevertheless exhibited normal physical growth.

Papilloma is a particularly rare form of tumor of the brain at all ages. In Tooth's [2] analysis of 258 cases of tumor of the brain examined at the National Hospital, London, in which the nature of the growth was verified by operation or autopsy, papilloma was found in only 3 instances. Davis and Cushing,[3] in a report of a series of 964 cases of verified tumors of the brain, 6 of which had originated from the choroid plexus, recorded that only about 20 examples of true papilloma of this structure were found in the literature up to 1924. Recently, Cushing,[4] in reporting a more complete series of 2,023 cases of tumor of the brain, cited 12 cases of this particular neoplasm, 6 of which were not included in the earlier report of 1924.

Consultation of the records of Bellevue Hosptial covering the entire service over a period of twenty years, since 1910, has revealed no mention of tumor of the choroid plexus.[4a]

According to Ewing,[5] the majority of subjects with the usual form of tumor of the choroid plexus (adenocarcinoma) are children or young adults.

Embryology and Histopathology.—Embryologically, the wall of the brain tube in certain sites is represented by a thin epithelial plate, the lamina chorioidea epithelialis. In the roof of the third and fourth ventricles and along an area on the medial walls of the hemispheres the epithelial lamina undergoes invagination toward the cavity of the ventricles, with pial tissue superimposed.[6]

Karsner [7] designated papilloma chorioideum as a papillary mass which springs from and is composed principally of the cells of the tufts. The

2. Tooth, H. H.: Brain **35**:61, 1912.

3. Davis, L. E., and Cushing, Harvey: Papillomas of the Choroid Plexus, Arch. Neurol. & Psychiat. **13**:681 (June) 1925; Tr. Am. Neurol. A., 1924, p. 365.

4. Cushing, Harvey: Intracranial Tumours, Springfield, Ill., Charles C. Thomas, Publisher, 1932, p. 8.

4a. Since the submission of this report, Charles A. Elsberg, in reporting a series of 878 verified intracranial tumors, has recorded the occurrence of 2 tumors of the choroid plexus (Bull. New York Acad. Med. **9**:1 [Jan.] 1933).

5. Ewing, James: Neoplastic Diseases, ed. 2, Philadelphia, W. B. Saunders Company, 1922, p. 418.

6. Villiger, Emil: Brain and Spinal Cord, edited by W. H. F. Addison, ed. 3, Philadelphia, J. B. Lippincott Company, 1925. Piersol: Cyclopedia of Medicine, Philadelphia, F. A. Davis Company, 1931, vol. 3, p. 774.

7. Karsner, H. T.: Human Pathology, Philadelphia, J. B. Lippincott Company, 1931, p. 968.

papillae, covered by cuboidal cells of the choroid plexus type, are superimposed on connective tissue. Absence of glia fibers and blepharoplasts aids in differentiating the choroid plexus papilloma from tumors of ependymal origin, which have cores of a glial character unlike the connective tissue of the tumors of the choroid plexus, and which rarely present villi or project into the ventricles.[8]

In 2 cases reported by Davis and Cushing,[3] papillomas in the lateral ventricles were associated with enveloping cysts.

Ewing [5] designated papillary adenocarcinoma as the usual form of tumor of the choroid plexus, noting that metastases indicative of malignancy sometimes occur in the pia or the brain tissue.

It is noteworthy that the tendency of such growths to cause a cerebrospinal fluid block was emphasized nearly a half century ago in a discussion by Robert T. Edes [9] on 4 cases characterized by encroachment of the tumor on the foramen of Monro.[10]

Symptomatology.—The fact that there may be no symptoms from tumors of the lateral ventricles until the growths have encroached on contiguous structures or produced some degree of occlusion of the ventricles has been emphasized by Cushing, and is well exemplified by the course in our case. As the neurologic picture becomes established, the list of possible symptoms and signs which may appear includes headache, dizziness, vomiting, convulsions, visual field defects, choked disks, hemiparesis and hemiplegia, dysarthria and sensory disturbances.

As observed not infrequently in the course of meningitis of infancy and as illustrated by the case here recorded, signs of a digestive disorder may for a considerable period exist without frank neurologic indications.

Diagnosis.—Meningitis, brain tumor or brain abscess is suggested in any infant who vomits persistently and in whose case pyloric obstruction and malformation of the digestive canal, such as diaphragmatic hernia and esophageal stricture, have been excluded.

Abnormal ocular appearances, increased tension of the fontanel and paralyses of various muscles call definitely for spinal puncture and, in addition, may call for subdural and ventricular taps.

Xanthochromic fluid without the characteristics of the fluid commonly found in meningitis is highly significant. The potentiality of

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8. Davidoff, L. M.: Brain Tumors, Utica, N. Y., State Hospital Press, 1931, p. 54.

9. Edes, R. T.: Tumors of the Choroid Plexus in the Neighborhood of the Foramen of Monro, M. News **52**:61 (Jan. 21) 1888.

10. Edes.[9] Förster, A.: Würzb. med. Ztschr. **5**:39, 1864. Stedman, J.: Boston M. & S. J. **109**:135, 1883. Wallman: Virchows Arch. f. path. Anat. **14**:385, 1858.

scurvy to cause a subdural hematoma with neurologic manifestations should, in this connection, be kept in mind.[11]

Intracranial pneumograms may help in localizing the tumor and the site of any existing cerebrospinal fluid block.

Prognosis.—Although a favorable outcome is not to be expected, even under competent and early applied surgical intervention, operation in skilled hands is apparently not an absolutely hopeless procedure (see Butterfield's case [1]).

Treatment.—Pending the application of radical surgical intervention, symptomatic measures to combat the failure of fluid intake and retention may serve to lower the operative risk. Repeated punctures to relieve intracranial tension are indicated. Lack of increased pressure of fluid withdrawn by spinal tap is a sufficient indication, in the presence of clinical signs of intracranial tension, for ventricular exploration.

SUMMARY

A case of papillary tumor of the choroid plexus in an infant is reviewed in conjunction with the citation of other reports of this condition.

A considerable review of the literature indicates that only about 30 cases of this condition duly verified by operation or by autopsy have been reported to date irrespective of the age period of the patients.

The possibility of confusing tumor of the brain with a primary gastric disorder in infancy is emphasized.

On the assumption that the incidence of ventricular tumor may be much higher than statistics suggest, diagnosis, prognosis and treatment are briefly considered.

11. Gilman, B. B., and Tanzer, R. C.: Subdural Hematoma in Infantile Scurvy, J. A. M. A. **99**:989 (Sept. 17) 1932.

Progress in Pediatrics

TUBERCULOSIS

I. INTERPRETATION OF ROENTGENOGRAMS OF THE CHESTS OF CHILDREN WITH TUBERCULOSIS; A CORRELATION OF THE ROENTGENOGRAMS OF FOURTEEN CHILDREN WITH CLINICAL AND PATHOLOGIC DATA

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The difficulty in the evaluation and interpretation of shadows seen in roentgenograms of the chests of a group of children enrolled in a clinic for tuberculous children and for those in close contact with tuberculous persons has prompted this study. In the region in which New Haven is located most children are subject to more or less frequent infections of the upper respiratory tract. Such children, as well as those with frank pulmonary infections, often show thoracic roentgenographic markings of one type or another which are difficult or impossible to differentiate from shadows caused by tuberculous lesions. In the roentgenograms of the chests of children reacting negatively to tuberculin, shadows are often seen which are similar in location and appearance to those observed in the roentgenograms of children reacting positively; the interpretation of the shadows is often influenced by a knowledge of the reaction of the patient to tuberculin. In order to discover any differential factors in comparable roentgenographic shadows caused by pathologic lesions of varied etiology, roentgenograms should be studied in the light of the case as a whole: first, in careful conjunction with the clinical history and laboratory data, and second, in relation to the postmortem observations. Anatomic control is of great importance

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This work was made possible by a grant from the William Wirt Winchester Fund, and represents part of a cooperative study on tuberculosis of the Research Committee of the National Tuberculosis Association.

and can hardly be overemphasized. Armand-Delille and other investigators [1] have advocated and carried out studies of this character.

In the study herewith presented the completed records, including roentgenograms, of fourteen tuberculous children on whom necropsies were performed are considered.[2] All but two of the children reacted positively to the intracutaneous injection of old tuberculin. (In case 7 the reaction was negative, and in case 14 there was no record.[3]) The majority of the cases studied were of generalized tuberculosis, but attention was focused on the pulmonary condition. We shall present the outstanding clinical and pathologic features in protocol notes, and show the last roentgenograms taken before death and, when possible, photographs of the pathologic specimens. The records in some cases go back a number of years, and the clinical notes were often inadequate and of little value. At times there were such discrepancies that it was difficult and sometimes impossible to make correlations with the roentgeno-

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1. Armand-Delille, P., and Lestocquoy, C.: Tuberculous Lobes in the Lungs of Infants, Gaz. méd. de France **2**:214 (May) 1928; The Diagnosis of Tuberculosis of the Tracheobronchial Glands, Am. J. Dis. Child. **38**:1125 (Dec.) 1929. Armand-Delille, P.: The Diagnosis of Tuberculosis of the Tracheobronchial Gland with Anatomic Control, ibid. **38**:648 (Sept.) 1929. Ross, S. G., and Crowdy, C. T.: Tuberculous Pyopneumothorax in an Infant Aged Five Months, ibid. **27**:456 (May) 1924. Gorter, E., and Lignac, G. O. E.: Collateral Inflammation of Lungs Around a Tuberculous Center, Acta pædiat. **10**:87 (Aug. 18) 1930. Farmer, H. L.: Ulcerative Pulmonary Tuberculosis in Infants, Am. J. Roentgenol. **12**:327, 1924. Ribadeau-Dumas: Tuberculose cavitaire du premier âge, Bull. et mém. Soc. méd. d. hôp. de Paris **36**:936, 1913; quoted by Siperstein, D. M., and Bauguess, Harry: Tuberculous Pulmonary Cavities in Infancy, Am. J. Dis. Child. **27**:586 (June) 1924.

2. After the manuscript of this paper was prepared another patient, a boy, aged 2 years, was admitted to the hospital with pulmonary tuberculosis. The patient died, and necrosy was performed. The case cannot be reported in detail, but the roentgenographic and postmortem observations are similar to those reported and discussed under group II. The roentgenogram showed an extensive shadow in the middle lobe of the right lung suggestive of consolidation, and throughout this shadow the bronchial tracings were well marked. Postmortem examination showed caseous tuberculous tracheobronchial lymphadenitis, caseous tuberculosis of the right lung, disseminated tubercles in both lungs and the spleen and liver and tuberculous meningitis. Acid-fast organisms were found in the exudate from the right ear.

3. For an evaluation of the reaction to tuberculin there should be taken into consideration the type of test (Pirquet, Mantoux) and the dosage (strength in milligrams of old tuberculin or in terms of dilution), as well as the descriptive data on the positive reaction (the extent of any erythema, edema, induration or necrosis).

grams. The latter also were sometimes unsatisfactory, having been made with varied technic and frequently under unfavorable conditions.[4]

Although the number of cases is small and the inadequacies in data are many, it is hoped that some ideas of value in the interpretation of roentgenograms may be suggested and a more critical study of roentgenographic evidence of tuberculosis in children stimulated.

Certain cases of nontuberculous bronchopneumonia in children—especially bronchopneumonia associated with infection with Bacillus influenzae and pneumococci group IV—present a roentgenographic picture difficult to differentiate from that often seen in proliferative tuberculosis. In addition, therefore, to the study here presented and just outlined, the roentgenograms of thirty children who had nontuberculous bronchopneumonia were examined; these roentgenograms are not discussed in this paper but were studied for purposes of comparison with those of the children with tuberculosis, and certain observations resulting from this study find expression in the general comment.

For comparative purposes, also, about forty roentgenograms of children with lobar pneumonia and about a hundred of adults were examined.

The patients have been classified into three groups: (1) six children with pulmonary tuberculosis with cavity formation; (2) four tuberculous children, three of whom had pulmonary tuberculosis without cavity formation, and one, chronic nontuberculous pneumonia; (3) four children in whom tuberculosis of the tracheobronchial lymph nodes was the predominant feature. The accompanying table gives a summary of the important thoracic anatomic lesions with a notation of their presence or absence clinically and roentgenographically.

4. As the result of experience, certain points in roentgenographic technic and procedure seem to us to be of special importance. They are as follows: 1. Roentgenograms should be taken with the chest in complete inspiration. It has been shown by Macklin and Hudson (by serial plates by Dr. Charles A. Macklin and by moving pictures by Dr. William A. Hudson at a meeting of the National Tuberculosis Association, Syracuse, N. Y., May, 1931) that among other changes during expiration, the hilus rises and broadens, assuming a contour quite different from that seen during inspiration. Failure to appreciate this has led, in our opinion, to many erroneous diagnoses of enlarged tracheobronchial lymph nodes. 2. Routine roentgenograms of the chest should be taken at 6 foot target-film distance; this, of course, is applicable only when the apparatus is sufficiently powerful and speedy to give an exposure adequate to reveal detail. We believe that many confusing and misleading shadows of the hilar and mediastinal regions would thus be eliminated, and a truer picture of this region would be obtained than is possible with a shorter target-film distance. 3. Oblique views of the chest are important for the diagnosis of involvement of the mediastinal region. They are especially enlightening when there are calcified lymph nodes in the peritracheal region. 4. In order to bring out calcium deposits clearly it is important that films be not underexposed ("soft"). 5. When possible, roentgenograms should be taken at various times during the course of the disease.

GROUP I: SIX CASES OF PULMONARY TUBERCULOSIS WITH CAVITIES

A diagnosis of pulmonary tuberculosis was established on the basis of clinical and roentgenographic findings. Though there were cavities in the lungs of the six children in this group, shadows indicative of

Correlation of Anatomic, Clinical and Roentgenographic Findings in the Thorax

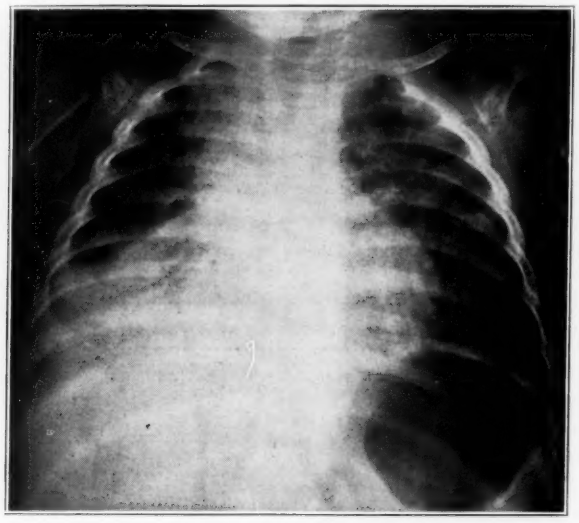
Group	Case		Anatomic Lesions	Clinical Evidence	Roentgenographic Evidence
I	1	Lungs	Pulmonary tuberculosis	+	+
			Cavity	0	+
			Bronchiectasis	0	+
		Lymph nodes	Enlarged and caseous	+	+
	2	Lungs	Pulmonary tuberculosis	+	+
			Cavity	0	+
		Lymph nodes	Enlarged, caseous and calcified	0	+
	3	Lungs	Pulmonary tuberculosis	+	+
			Cavity	+	+
			Bronchiectasis	+	+
			Pleural effusion	+	+
		Lymph nodes	Enlarged and caseous, right	+	+
	4	Lungs	Pulmonary tuberculosis	+	+
			Cavity	+	+
			Bronchiectasis	0	0
		Lymph nodes	Slightly enlarged and caseous	0	0
	5	Lungs	Pulmonary tuberculosis	+	+
			Cavity	0	+
			Bronchiectasis	0	0
		Lymph nodes	Enlarged, caseous, with pressure on trachea and left bronchus	+	+
	6	Lungs	Pulmonary tuberculosis	+	+
			Cavity	0	0
			Bronchiectasis	+	+
		Lymph nodes	Enlarged, caseous and necrotic	0	0
II	7	Lungs	Pulmonary tuberculosis	+	+
		Lymph nodes	Enlarged, caseous and necrotic	0	0
	8	Lungs	Pulmonary tuberculosis	+	+
		Lymph nodes	Enlarged and caseous	0	0
	9	Lungs	Pulmonary tuberculosis	0	0
		Lymph nodes	Caseous and calcified	0	+
	10	Lungs	Nontuberculous, interstitial pneumonia	+	+
		Lymph nodes	Nontuberculous	0	0
III	11	Lungs	Disseminated tubercles, acute bronchopneumonia, right	+	+
		Lymph nodes	Enlarged and caseous	+	+
	12	Lungs	Few disseminated tubercles	0	0
		Lymph nodes	Enlarged and caseous	0	+
	13	Lungs	Pulmonary tuberculosis	+	+
			Left, emphysema	+	+
		Lymph nodes	Slightly enlarged and caseous	+	0
	14	Lungs	Pulmonary tuberculosis	+	+
			Bronchiectasis	0	+
		Lymph nodes	Enlarged and caseous; erosion of bronchus by gland	0	0

them were obvious in the roentgenograms of only four (cases 1, 2, 3 and 4). A shadow which might be interpreted as indicative of cavity formation was present in the roentgenogram of the fifth child (case 5). Such an interpretation was not made, however. No indication of the presence of a cavity was present in the roentgenogram of the sixth

child (case 6). Outlines of dilated bronchi surrounded by a shadow indicative of consolidated lung were clearly shown in the roentgenograms of three children (cases 1, 3 and 6).

CASE 1.—*Tuberculous tracheal lymphadenitis; chronic pulmonary tuberculosis; tuberculous bronchiectasis with cavities; disseminated visceral tuberculosis; tuberculous meningitis.*

History.—M. A., a girl, was admitted to the hospital at the age of 9 months; the age at death was 11¼ months. The tuberculous contact was not known.



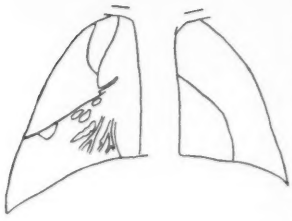


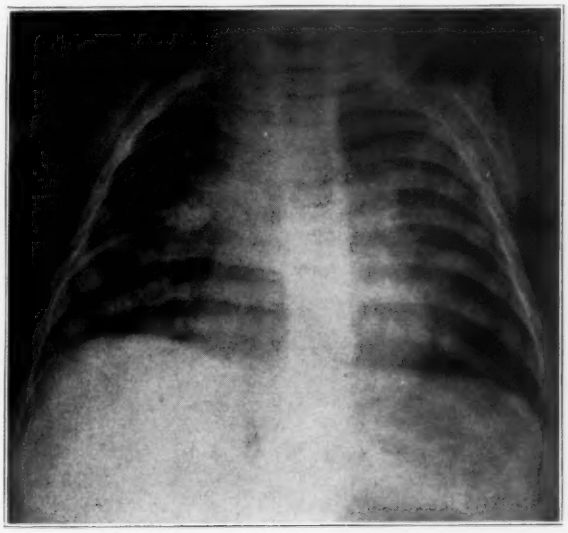
Fig. 1 (case 1).—Roentgenogram taken on July 26, 1928, ten weeks before death. The chest is in partial expiration; the trachea is deviated to the right. The right side of the chest shows a heavy shadow at the base with bronchiectatic markings and a large shadow bulging from the mediastinum, with a fainter shadow extending above into the apical region. The left side of the chest shows miliary shadows.

The patient was born on Oct. 27, 1927. The weight at birth was 9½ pounds (4.3 Kg.). She was breast-fed for two weeks; thereafter, inadequate and irregular artificial feeding was given. In April, 1928, she had pneumonia on the right side for two weeks, with recovery. In June, furunculosis of the scalp developed.

Two weeks before admission the patient had fever, cough, rapid respiration and loss of weight. Four days before admission (July 23, 1928) she was seen in New Haven Hospital Dispensary, where a diagnosis of "pneumonia" was made. On the day of admission, she was seen by an outside physician and was thought to have empyema.

The patient was in the hospital from July 27 to Oct. 3, 1928 (ten weeks).

Examination on Admission.—The child was irritable, pale, malnourished and dehydrated, with rapid respirations and an occasional cough; there were papulopustular rash on the trunk, general glandular enlargement and enlargement of the liver and spleen. There was poor expansion over the upper lobe of the right lung. The right lung was dull to percussion; the breath sounds were diminished under the scapula, tubular at the base and flat to percussion. The front of the left lung was hyperresonant to percussion; the back, impaired; the breath sounds were everywhere diminished.



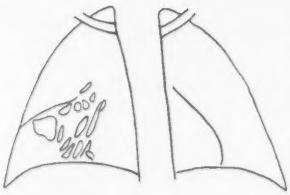


Fig. 2 (case 1).—Roentgenogram (light plate) taken on Sept. 14, 1928, three weeks before death. The chest is rotated a little to the right, with the trachea deviated to the right. The right side of the chest shows in the lower lobe, which is fenestrated with bronchiectic markings, one large cavity, and a hazy upper lobe, with a mediastinal shadow of indefinite outline pyramiding along the interlobar septum. The left side of the chest is hazy, with generalized miliary shadows which are most marked in the hilar region.

Clinical Course.—The weight on admission was 5.7 Kg.; there was no gain during the patient's stay in the hospital. The temperature was elevated and irregular, with a swinging curve. There was a gradual definite loss of strength; the appetite was poor. There was furunculosis for which frequent incisions were made. Bilateral purulent otitis media was present. There was little cough or sputum. Clubbed fingers developed. Three weeks before death, signs of meningeal irritation, vomiting, retraction of the head, stiffness of the neck, right facial paralysis and rigidity of the right side of the body developed; the deep reflexes

were increased. The pulmonary signs gradually increased, with tubular breath sounds in the interscapular region and toward the base of the right lung, with suppression at the extreme base and occasional râles. The left side, as before, was hyperresonant to percussion; the diminished breath sounds became very loud. The patient had a "metallic cough."

Laboratory Data.—The reaction to 0.01 mg. of tuberculin was positive. On admission the white blood cells numbered 18,200, with 64 per cent polymorphonuclears. On August 29, a smear of the sputum was negative; inoculation into a guinea-pig gave positive results for tubercle bacilli. On September 24 and 28, the spinal fluid contained 50 and 200 cells, respectively; the reaction for globulin was positive. On September 20, the ventricular fluid contained 84 cells; the reaction for globulin was positive; tubercle bacilli were seen.

Fig. 3 (case 1).—The right lung. The upper lobe is atelectatic and shows tubercles; the lower lobe shows chronic ulcerative pulmonary tuberculosis with dilated ulcerated bronchi and cavities. There are large caseous peritracheal lymph nodes.

Roentgen Observations.—Eight roentgenograms were taken between July 26 and Sept. 28, 1928. The first film (taken on July 26, fig. 1) showed bilateral generalized miliary shadows, an extensive shadow in the lower lobe of the right lung traversed by outlines of dilated bronchi and a large shadow extending outward from the right of the mediastinum. The film taken on September 14 (fig. 2), three weeks before death, showed enlargement and intensification of the shadows seen in the first film; the outlines of the dilated bronchi were more striking, and the presence of a large cavity in the lower lobe of the right lung was clearly indicated.

Postmortem Examination (Complete) (fig. 3).—The lower lobe of the right lung showed chronic ulcerative pulmonory tuberculosis with dilated bronchi and

cavities; the upper lobe was compressed by a large peritracheal mass of nodes; the upper middle lobes contained conglomerate tubercles. The left lung showed disseminated miliary tubercles. The pleurae were clear. The lymph nodes on the right showed caseous peritracheal lymphadenitis, with calcium salts and a mass 6 by 2 by 2.5 cm. There were ulcerative tuberculous ileocolitis, tuberculous appendicitis, disseminated tubercles in the viscera and small succulent abdominal nodes. Tuberculous meningitis and multiple tuberculomas in the brain were found.

Bacteriology.—A film formed in the spinal fluid, in which many acid-fast organisms were found.

Comment.—The clinical history and findings in this case established a diagnosis of pulmonary tuberculosis. The roentgenograms (figs. 1 and 2) showed small bilateral disseminated shadows. A large shadow in the lower half of the right lung with linear and circular tracery indicated consolidation with dilated bronchi and cavity formation. There was a clinical report of "metallic cough" and of clubbed fingers. The mediastinal shadows in the earlier of the eight films taken suggested the presence of enlarged tracheobronchial lymph nodes. The postmortem examination was confirmatory of the roentgenographic interpretation; there were found (fig. 3) miliary tuberculosis, tuberculous pneumonia with bronchiectasis and cavity formation in the right lung and tuberculous tracheobronchial lymphadenitis.

CASE 2.—*Tuberculous mesenteric, retroperitoneal and tracheobronchial lymphadenitis; chronic pulmonary tuberculosis with cavity formation; fibrinous pleurisy at the apex of the left lung; ulcerative tuberculous ileocolitis; tuberculous peritonitis and salpingo-oophoritis; disseminated tubercles in the viscera; tuberculous meningitis.*

History.—M. L., a girl, was admitted to the hospital at the age of 14 months; death occurred nine days later. The tuberculous contact was not known.

The patient was born on Aug. 1, 1927. The weight at birth was "10 pounds" (4.5 Kg.). She was breast-fed. She had always been weak.

For two weeks before admission there was increasing irritability, with crying, drowsiness, persistent vomiting, constipation, loss of weight and "some cough."

The patient was in the hospital from September 28 to Oct. 6, 1928 (nine days).

Examination on Admission.—The child was drowsy; there was evidence of recent loss of weight. The breath sounds were harsh at the back of the lower lobe of the left lung, with prolonged expiration. There was a mass in the right lower quadrant. A vaginal discharge was noted. The reflexes were hyperactive.

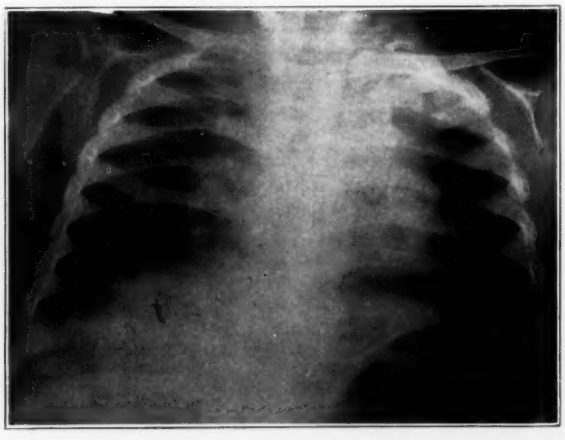
Clinical Course.—The weight was 8 Kg. The fever, which was usually between 37 and 38 C. (98.6 and 100.4 F.), rose to 40.2 C. (104.3 F.) on the day of death. The course was downhill, with increased drowsiness, poor appetite and occasional vomiting. There were fine râles in the chest. The reflexes were hyperactive; there was a bilateral ankle clonus. The patient had a convulsion in the last three hours of life, the hands and feet being in carpopedal spasm. There was ptosis of the left eyelid; the neck was not stiff; there was no Kernig sign; the fontanel was not bulging.

Laboratory Data.—The reaction to 0.02 mg. of tuberculin was positive. On admission the white blood cells numbered 17,800, with 75 per cent polymorpho-

nuclears. A vaginal smear was negative for gonococci. On September 28, the spinal fluid contained 130 cells; the Pandy reaction was 4 plus; on October 2, it contained 133 cells; inoculation into a guinea-pig caused tuberculosis.

Roentgen Observations.—Only one roentgenogram was taken, on Sept. 28, 1928, nine days before death (fig. 4); it showed a shadow at the apex of the left lung within which was a circumscribed area of decreased density suggestive of cavity. Shadows of calcific deposits showed in the left lower cervical and paramediastinal regions. Rather extensive infiltration of the right lung was indicated.

Postmortem Examination (Complete) (fig. 5).—The upper lobe of the left lung showed chronic pulmonary tuberculosis with a cavity at the apex 2 cm. in



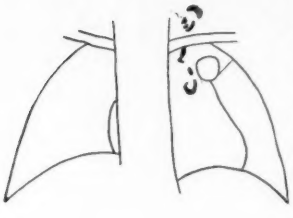


Fig. 4 (case 2).—Roentgenogram taken on Sept. 28, 1928, nine days before death. The chest is in expiration and is rotated slightly to the left. The left side of the chest shows a shadow at the apex, with an outlined area of slightly less density between the first and second ribs (cavity); in the paramediastinal shadow in this area are a few fine spots of greater density (calcium). In the right side of the chest there is some increase over the normal hilar shadows, with a hazy appearance of the upper region. In the left lower cervical region are two circumscribed areas of sharply outlined mottled density (calcium).

diameter and filled with thick, yellow, purulent material; above the cavity was a calcifying and caseous mass, 1.5 cm. in diameter, with fibrinous pleurisy at the apex; the lower lobe showed disseminated proliferative miliary tubercles; the pleura was clear. The right lung showed diffuse disseminated proliferative tubercles; the pleura was clear. There were peritracheal caseous lymphadenitis, left peribronchial calcified and caseous lymph nodes and a mass 2 by 2 by 3 cm.; the left cervical lymph nodes were caseous and calcified, and were more than 1 cm. in diameter; there was mesenteric and retroperitoneal tuberculous caseous lymph-

adenitis. Chronic tuberculous peritonitis and salpingo-oophoritis, ulcerative ileocolitis and disseminated tubercles in the viscera were noted. There were tuberculous meningitis and multiple tuberculomas of the brain.

Comment.—The clinical data as to the thoracic signs and symptoms were unfortunately too meager to be of value. The one roentgenogram,

Fig. 5 (case 2).—The left lung. At the apex is pulmonary tuberculosis, with a cavity filled with débris. The lower lobe contains disseminated tubercles; there is a large caseous and calcified peribronchial lymph node.

taken on the day of admission (fig. 4), indicated a zone of consolidation in the apex of the left lung. Within this shadow, the area of slightly decreased density suggested the possibility of cavity even though it was not absolutely clearcut. If during the child's stay in the hospital the

cavity was filled with caseous material (as was found to be the case at necropsy, fig. 5), the explanation both of the lack of striking clinical signs and of the clarity of the film as regards cavity is obvious.

The shadows in the right lung were suggestive of zones of consolidation. Necropsy revealed the presence of these zones and that they were tuberculous.

The calcific deposits in the cervical and thoracic regions showed clearly the presence of tuberculous nodes. The chest was held in expiration, and hence the contour of the mediastinum, although suggestive of a large mass, was too distorted to justify a diagnosis of tracheobronchial lymphadenitis.[4]

CASE 3.—*Tuberculous mesenteric, retroperitoneal and tracheobronchial lymphadenitis; caseous pulmonary tuberculosis with bronchiectasis and cavity formation; tuberculous pleurisy; tuberculous ulcerative enterocolitis; disseminated tubercles in the viscera.*

History.—B. J., a girl, was admitted to the hospital at the age of 10 months; the age at death was 1 year. The child had been living for seven months in the house with an uncle who had pulmonary tuberculosis.

The patient was born on Jan. 7, 1931. The weight at birth was 8 pounds (3.6 Kg.). The patient was breast-fed for two months.

In August, 1931, at the age of 7 months, the patient had "croup and bronchitis," and had coughed more or less since then. For the past week (or longer?) she had had diarrhea; she vomited three times, and she had been restless, had little appetite and had lost weight.

The patient was in the hospital from Nov. 7, 1931, to Jan. 10, 1932 (two months).

Examination on Admission.—The weight was 5,460 Gm. The temperature was 38 C. (100.4 F.). The patient was a poorly developed, extremely malnourished, irritable and chronically sick child. She had a loose productive cough and mild rhinopharyngitis. The upper lobe of the right lung was dull, with diminished slightly high pitched breath sounds; the left lung was hyperresonant. The abdomen was distended and boardlike, with many small easily palpable masses; the liver was down two fingerbreadths.

Clinical Course.—The curve for the weight oscillated, with practically little change in the level. There was a constant fever with a swinging curve, usually between 38 and 39 C. (100.4 and 102.2 F.). There was a persistent loose productive cough. The pulmonary signs increased, spreading over the entire right side; râles were variable over both lungs. On November 28, signs of cavity were found in the right axilla. On December 9, there was a decrease in respiratory excursion of the right side with signs of fluid at the base of the right lung; there were distant bronchial breath sounds on the left. There were clubbing of the fingers and toes and bilateral purulent otitis media. On December 25, there were no meningeal signs. The diarrhea ceased soon after admission, but reappeared a few days before death; in the intermission, the stools were "normal." The appetite was always poor, with some vomiting, especially toward the end of life.

Laboratory Data.—The reaction to 0.2 mg. of tuberculin was positive. The red blood cells numbered 4,480,000; the white blood cells, 17,500, with 78 per

cent polymorphonuclears. Inoculation of sputum (stomach washings) and pus from the right ear into a guinea-pig gave acid-fast bacilli.

Roentgen Observations.—Roentgenograms were taken on Nov. 7, 9 and 30, 1931. The first two films showed extensive shadows over the entire right lung, slightly less dense at the apex and base. There was a "pleural line" on this side. The left lung showed "fluffy" shadows extending from the hilus to the periphery, the apex and base being relatively clear. The roentgenogram taken on November 30 (fig. 6), six weeks before death, showed an extensive shadow on the right lung, exempting the base and apex. There was a pleural line within the shadow,

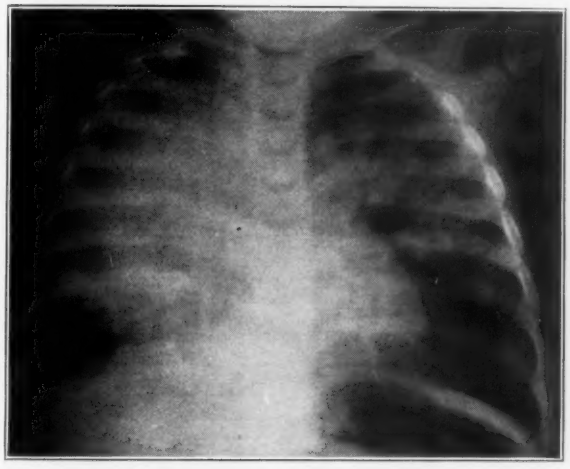


Fig. 6 (case 3).—Roentgenogram taken on Nov. 30, 1931, six weeks before death. The right side of the chest shows a dense shadow occupying the whole lung except the apical and peripheral basilar regions, with bronchectatic markings at the base and a cavity in the middle lobe; there is a fluid shadow along the periphery of the whole lung, and a demarcated dense shadow to the right of the mediastinum. The left side of the chest shows fluffy confluent shadows.

and there were oval and tubular markings. There were extensive shadows in the left lung as described for the preceding films.

Postmortem Examination (Partial) (fig. 7).—The right lung showed extensive caseous tuberculosis in all lobes, with less involvement at the apex and a cavity in the upper part of the middle lobe, 2.5 by 2 by 2 cm., partially filled with caseous débris. In the left lung the caseous tuberculosis was more marked in the lower lobe. There was ulcerative tuberculous bronchitis in both lungs, with bronchiectasis in the middle lobe of the right lung. There were 150 cc. of fibrinopurulent fluid and numerous fibrinous adhesions in the right pleural cavity; the left showed fibrinous diaphragmatic pleurisy; the rest of the left pleura was clear. The tracheobronchial nodes on the right were greatly enlarged and caseous

and contained a mass several centimeters in diameter with a single peribronchial node 1 cm. in diameter; the cervical, mesenteric and retroperitoneal lymph nodes were caseous, some showing slight calcification. Tuberculous ulcerative enterocolitis and disseminated tubercles in the pericardium, spleen, liver and kidneys were noted.

Comment.—The tuberculous etiology of the disease in this child was determined clinically from a history of contact and the clinical and laboratory findings. The roentgenogram (fig. 6), taken six weeks before death, was interpreted as indicative of tuberculous consolidation with cavity formation, bronchiectasis and pleurisy on the right; there were areas of consolidation on the left. This interpretation was demonstrated at necropsy to be correct (fig. 7). The lesions in the right lung

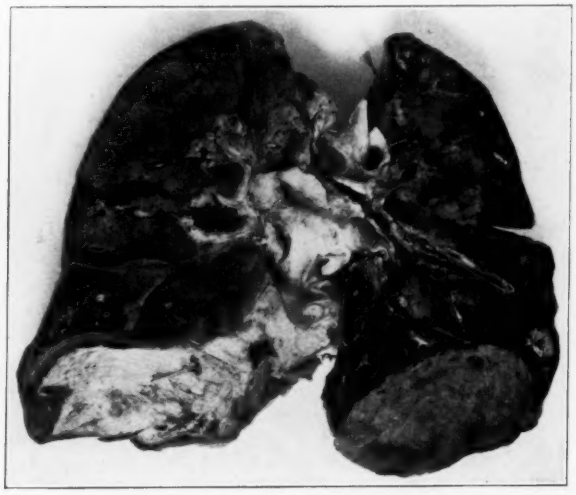


Fig. 7 (case 3).—The lungs and lymph nodes. The right lung shows caseous pulmonary tuberculosis, bronchiectasis and a cavity in the middle lobe with fibrous pleural adhesions. The left lung shows focal caseous pulmonary tuberculosis and diaphragmatic fibrinous pleurisy. The right lymph nodes are enlarged and caseous.

at necropsy were more extensive than indicated in the roentgenogram, but the disease progressed, of course, in the six weeks between the date of the taking of the roentgenogram and that of the postmortem examination.

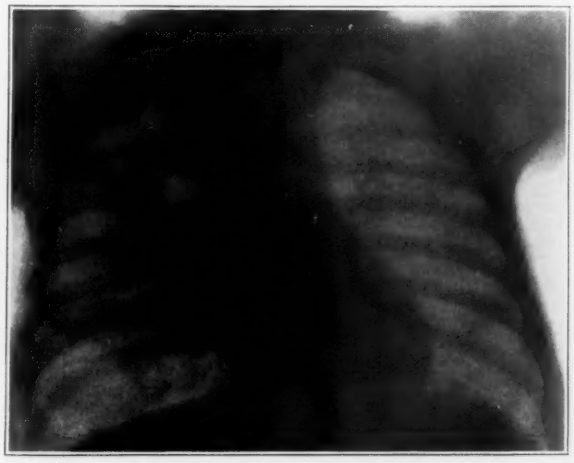
CASE 4.—*Tuberculous mesenteric and tracheobronchial lymphadenitis; pulmonary tuberculosis and bronchiectasis with cavity formation; pleural adhesions (right); tuberculous enteritis; disseminated tubercles in the viscera; tuberculous meningitis.*

History.—D. S., a boy, was admitted to the hospital at the age of 8 months; the age at death was 9 months. The tuberculous contact was not known.

The patient was born on May 13, 1921. He was breast-fed for three months and then was given complementary feedings. There was frequent vomiting. The weight at the age of 5 months was 15 pounds (6.8 Kg.), and at 8 months, 14 pounds (6.4 Kg.). He had had "bronchial asthma" since the second month of life. He had had purulent otitis media, most frequently on the left side, since 5 months of age.

On Jan. 3, 1922, tenderness of the left mastoid developed.

The patient was in the hospital from January 11, to Feb. 19, 1922 (five and one-half weeks).



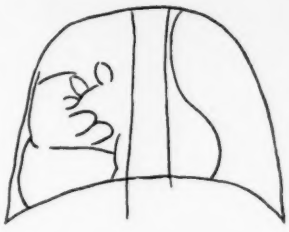


Fig. 8 (case 4).—Roentgenogram taken on Jan. 30, 1922, three weeks before death. (This reproduction is a contact print from a roentgenogram; therefore, the dark and light areas are the reverse of those seen in the photograph of a roentgenogram.) There are shadows indicative of consolidation in the middle and upper lobes of the right lung, with evidence of extensive cavity formation. The appearance of the base of the right lung is indicative of over-aeration rather than of a cavity. The right pleural line and interlobar septum are seen. The left side of the chest shows a general haziness.

Examination on Admission.—The skin was dry. The pharynx was slightly red. There was a fluctuating tumor of the left mastoid. There were harsh, vesicular breath sounds, but no tubular breathing or râles; he had a loose cough. The spleen was large.

Clinical Course.—On January 8 the patient weighed 6,060 Gm. He lost 1 Kg. during his stay in the hospital. The fever varied from 37 C. to 39.8 C. (98.6 to 103.6 F.). On January 11, mastoidectomy was performed on the left side; a caseous node and a granulating sinus were found at the side of the wound. Healing of the wound did not take place. On January 14, dulness of the upper lobe

of the right lung, râles and harsh breath sounds were noted. Tuberculids were present. Stiffness of the neck was noted. The patient was fed by gavage because of persistent vomiting. He had a constant cough. The pulmonary signs increased, with dulness, râles and bronchial breath sounds on the right and emphysematous changes on the left. On January 27, there were cavernous breath sounds and flatness over the second and third right interspaces, with loud râles; there was left facial paralysis, with slight strabismus and ptosis.

Laboratory Data.—The reaction to 0.02 mg. of tuberculin was positive. On admission, the white blood cells numbered 17,200. On Jan. 15, 1922, a blood

Fig. 9 (case 4).—The right lung. There is caseous pulmonary tuberculosis with a cavity in the middle lobe.

culture was negative, and sputum was positive for tubercle bacilli. On January 14, the spinal fluid contained 50 cells, but no globulin.

Roentgen Observations.—Roentgenograms were taken on January 15, 24 and 30 and February 6. The first showed a shadow in the upper and middle lobes of the right lung, with areas of decreased density in the middle of the shadow, indicative of extensive multilocular cavity formation. There was a pleural line on the right; the left pulmonary field indicated some infiltration. The film taken on January 30 (fig. 8) showed some extension of the shadows. The last film (taken on February 6, two weeks before death) indicated no essential change.

Postmortem Examination (Complete) (fig. 9).—The left lung showed conglomerate tubercles throughout; the pleura was clear; the bronchi were filled with mucus. The right lung was completely consolidated, with a large cavity in the

middle lobe occupying most of the lobe and peripherally situated; the wall of the cavity was thick, containing grayish-yellow material, with ragged edges projecting into the cavity; a slender fibrous cord of obliterated vessel stretched across the cavity; the bronchial lumens were mostly obliterated by yellow opaque necrotic material; there was necrotizing bronchitis; the pleura showed dense fibrous tuberculous adhesions. There were caseous tracheobronchial and mesenteric lymphadenitis, tuberculous ulcerative enteritis, disseminated tubercles in the skin (tuberculids) and in the parenchymatous organs, tuberculous meningitis and chronic suppurative mastoiditis (apparently nontuberculous).

Bacteriology.—Tubercle bacilli were found in histologic sections of the lungs and skin; inoculation of the mesenteric lymph nodes was positive for tuberculosis in a guinea-pig and negative in a rabbit.

Comment.—In this case, that of a boy of 8 months, there was a history of "bronchial asthma" since the age of 2 months. The clinical diagnosis of pulmonary tuberculosis with cavity made at the time of admission was supported by the roentgenograms. During the child's stay in the hospital the reports on four films taken at weekly intervals mentioned the generalized mottled shadows on both sides, which were most marked in the upper and middle lobes of the right lung, and the large multilocular areas of decreased density in the middle lobe on the right side. The reproduction here given (fig. 8) is of the film taken on January 30, three weeks before death.

At necropsy there were extensive consolidation of the right lung (fig. 9), a multilocular cavity with ragged edges and bridges of fibrous cords. Necrotizing bronchitis and dense fibrous pleural adhesions were found. The left lung showed zones of consolidation. In respect to these findings, the roentgenographic interpretation was in agreement. The base of the right lung, which was aerated, according to the roentgenogram, was found consolidated at necropsy, but the interval between the taking of the roentgenogram and necropsy was three weeks.

CASE 5.—*Tuberculous mesenteric, tracheobronchial and cervical lymphadenitis; pulmonary tuberculosis and bronchiectasis with cavity formation; pleural adhesions; tuberculous peritonitis and salpingo-oophoritis; disseminated tubercles in the viscera.*

History.—R. R., a girl, was admitted to the hospital at the age of 17½ months; the age at death was 20½ months. The tuberculous contact was not known.

The patient was born on April 1, 1923. The weight at birth was "6½ pounds" (2.9 Kg.). She was breast-fed for two weeks; subsequently unboiled milk and various artificial foods were given. She vomited at times; she had recurrent diarrhea with acute exacerbations and with blood-streaked stools in July for one week. Respiratory infections occurred frequently; she had "bronchitis" at the age of 8 months and whooping cough at 9 months with "fever off and on for six months."

For about three weeks there were diarrhea with mucus, occasional vomiting and an increase in the size of the abdomen. There was a loss of appetite, with a loss of weight. The patient showed apathy for a few days.

She was in the hospital from Sept. 17 to Dec. 14, 1924 (three months).

Examination on Admission.—The patient was a pale, poorly developed and emaciated child. The abdomen was enlarged (57 cm.) and tense, with a fluid wave and shifting dulness. The chest was thin. The lower interspaces of the lungs were retracted during inspiration. On the right, the breath sounds were diminished in front; there were a few coarse râles at the base. The upper lobe of the left lung showed dulness, loud, harsh breath sounds and a few coarse râles. The diaphragm was high (because of the size of the abdomen).

Clinical Course.—On admission the patient weighed 8.2 Kg.; at death, 5.5 Kg. The temperature was only slightly elevated, but had a swinging curve. The appetite was poor; there was increasing weakness, with a loss of weight. The diarrhea ceased after three weeks, and the girth of the abdomen decreased to

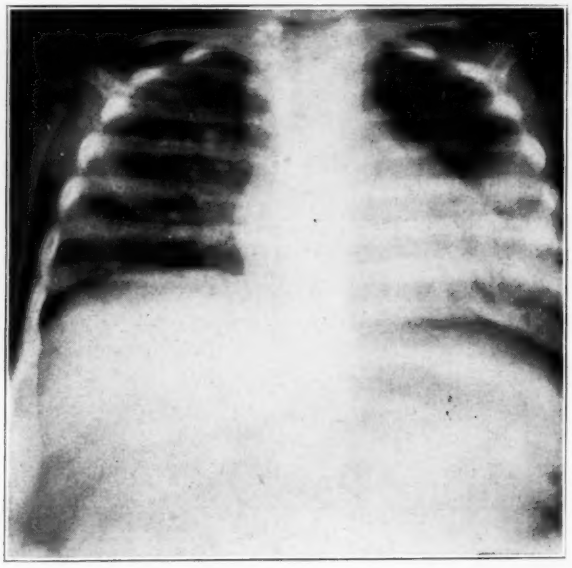
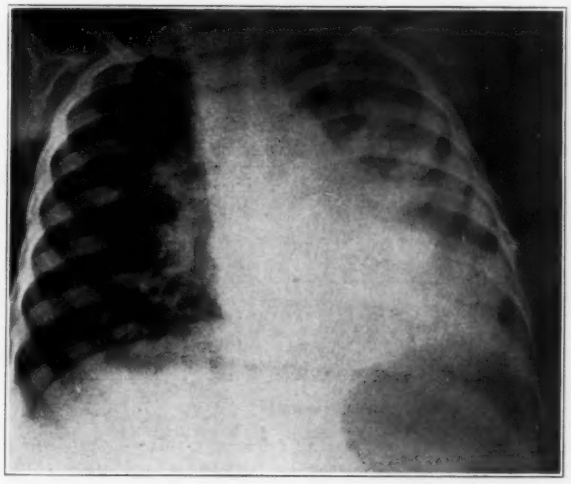


Fig. 10 (case 5).—Roentgenogram taken on Oct. 11, 1924, two months before death. The chest is in expiration. The left side of the chest shows the upper lobe well aerated (cavity); the lower lobe shows a dense shadow with slight variations in density. The right side of the chest shows a general haziness, with mottling in the lower inner zone; the right mediastinal shadow is wide.

44.5 cm. on October 22. The spleen and large masses became palpable in the abdomen. There were bilateral purulent otitis media and acute cervical adenitis. Cough developed. The lungs showed marked retraction of the interspaces, especially at the bases, and at the left more than the right. The breath sounds on the right were harsh, short and jerky, with coarse râles. The left side was dull to percussion; the breath sounds were diminished, short and jerky, with consonating râles; at times very little air passed into the lung.

Laboratory Data.—The reaction to 0.1 mg. of tuberculin was positive. On admission, the white blood cells numbered 15,900, with 78 per cent polymorphonuclears. The sputum was negative for tubercle bacilli on two examinations.

Roentgen Observations.—Roentgenograms were taken on Sept. 19, Oct. 11 and Dec. 13, 1924. The first film (fig. 10) was interpreted as showing a shadow of consolidation in the lower lobe of the left lung and a clear, well aerated upper lobe. The film taken on December 13 (fig. 11), the day before death, showed spread of the shadow in the lower lobe of the left lung, with a stippled area of calcification; there was a marked increase in the trunk markings in the upper lobe. There was evidence of rather extensive infiltration in the right paramediastinal region.



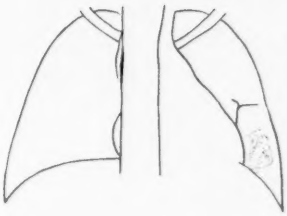


Fig. 11 (case 5).—Roentgenogram taken on Dec. 13, 1924, the day before death. The chest is in expiration and is rotated somewhat to the left. The left side of the chest shows the upper lobe well aerated (cavity), with faint trunk markings; there is a heavy mottled shadow in the rest of the lung, which is more dense in the mesial and basilar zones; near the base is a circumscribed area with stippling (calcium). The right side of the chest shows a moderate increase in the amount and density of the normal hilar trunk shadows. The mediastinum shows moderate bilateral widening.

Postmortem Examination (Partial).—The right lung was normal except for a calcified node in the lower lobe; the left lung showed ulcerative exudative and proliferative pulmonary tuberculosis. There was a cavity in the upper lobe of the left lung, 6 by 5 by 3 cm., filled with fluid and necrotic material, fibrous strands of vessels and bronchi. The left bronchus showed ulcerative tuberculous bronchitis, most marked in the left upper lobe and with bronchiectactic cavities in the lower lobe. The right pleura showed adhesions with an apical scar; the left, adhesions with a calcified plaque on the left lower pleura. There were tuberculous cervical and mesenteric lymphadenitis and bilateral tuberculous peri-

bronchial and peritracheal lymphadenitis. At the hilus there was a collar of caseous nodes compressing the trachea and the left bronchus. The largest nodes measured 2.5 by 3 cm. and 0.5 by 1 cm. There were disseminated tubercles in the viscera, with tuberculous peritonitis and tuberculosis of the uterus, ovaries and tubes.

Bacteriology.—B. tuberculosis was found (histologically).

Comment.—In the film taken on October 11 (fig. 10) the upper lobe of the left lung was uniformly dark, as though it was emphysematous, but nothing was definitely outlined to suggest a cavity. In the film taken two months later (December 13, fig. 11), the day before death, somewhat exaggerated linear shadows appeared traversing this area; these destroyed the uniformly dark appearance in this region seen in the first film. At necropsy there was found here a huge cavity filled with débris and traversed by fibrous strands of vessels and bronchi. The compression of the left bronchus by the collar of lymph nodes and the consequent diminution in respiratory exchange may, in part, have explained the lack of clinical evidence of cavity and accounted for the observation that at times little air passed into the left lung.

The clinical and roentgenographic evidences of consolidation of the lower lobe of the left lung and deposition of calcium in the pleura were confirmed at necropsy.

Although in the roentgenogram taken on October 11 (fig. 10) there was a distortion of the thoracic contents owing to elevation of the diaphragm (the patient had peritonitis), and in that taken on December 13 (fig. 11) there was some rotation of the chest, in both films the mediastinal shadow, nevertheless, was seen to be of abnormal shape and width. This fact, coupled with the clinical evidence of pressure by the tracheobronchial lymph nodes, would indicate extensive lymphadenitis. This diagnosis was supported by the necropsy.

CASE 6.—*Tuberculous mesenteric, tracheobronchial and cervical lymphadenitis; tuberculous pneumonia and bronchiectasis with cavity formation; tuberculous pleurisy; disseminated tubercles in the viscera.*

History.—J. S., a boy, was admitted to the hospital at the age of 14 months; death occurred one week later. The tuberculous contact was not known.

The patient was born on Feb. 5, 1923. The weight at birth was "9½ pounds" (4.3 Kg.). He was breast-fed for a time; then supplementary milk was given.

Three and one-half months before admission the patient had "tonsillitis, cold on chest, and fever—104.5 F. at the beginning"; he was ill for four weeks. Six weeks before admission he had noisy breathing; one week later, high fever, from 103 to 104 F., was noted, which lasted for three weeks. Since then, he had had persistent fever, cough and occasional vomiting. Thoracentesis (without result) was carried out five days before admission. The patient had not appeared ill at any time.

The patient was in the hospital from April 3 to 10, 1928 (eight days).

Examination on Admission.—The weight was 8 Kg. The child was pale, fairly well nourished and very active, and he had a cough. The pharynx was slightly red; the liver and spleen were enlarged. The right lung showed slight expansion, with dulness over the upper lobe and flatness at the base; the breath sounds were distant and diminished, with occasional râles. On percussion the left lung was found to be hyperresonant; the breath sounds were loud and harsh.

Clinical Course.—The temperature was elevated, and had a swinging curve. The child showed constant activity, poor appetite, a persistent cough and dyspnea. The "fluid signs changed to those of consolidation" on the right, with an increase of râles. There was a terminal respiratory crisis, with restlessness, coughing, dyspnea and cyanosis.

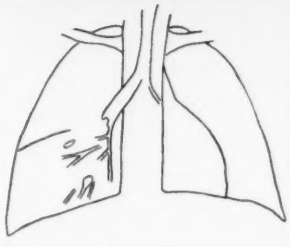


Fig. 12 (case 6).—Roentgenogram taken on April 4, 1923, one week before death. There is a heavy shadow over the lower lobe of the right lung, with bronchiectatic markings. The apex of the right lung and the left lung are clear. No cavity is evident.

Laboratory Data.—The reaction to 0.02 mg. of tuberculin was positive. On admission, the white blood cells numbered 14,400, with 67 per cent polymorphonuclears. A pleural tap was dry on admission.

Roentgen Observations.—Roentgenograms were taken on April 4 and 9, 1924. The first (fig. 12), taken the day after admission, showed a homogeneous shadow in the lower lobe of the right lung transversed by distinct outlines of the bronchi, but without a suggestion of cavity formation. The film taken on April 9, the day before death, showed a shadow occupying the entire right lung, which was less dense at the apex.

Postmortem Examination (Partial) (fig. 13).—The right lung showed acute tuberculous bronchopneumonia, which was more marked in the middle and lower

lobes, and generalized tuberculous ulcerative bronchitis; the lower lobe showed tuberculous caseous pneumonia with a cavity; the upper lobe, caseous miliary tubercles. The upper lobe of the left lung was clear; the lower lobe showed caseous miliary tubercles. The pleurae showed bilateral fibrinous pleurisy. There was bilateral tuberculous tracheobronchial lymphadenitis; the nodes measured from 3 to 10 mm., and contained caseous centers; tuberculous cervical and mesenteric lymphadenitis was noted. There were disseminated tubercles in the viscera.

Comment.—The noteworthy roentgenographic findings in this case were indicative of consolidation of the lower two thirds of the right

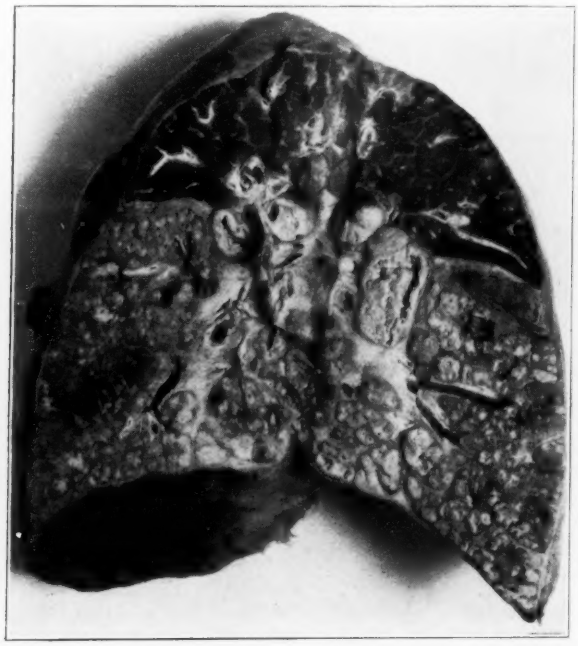


Fig. 13 (case 6).—Longitudinal section of the right lung. There is tuberculous caseous pneumonic consolidation of the middle and lower lobes, with ulcerative tuberculous bronchiectasis and a cavity. The upper lobe shows scattered caseous miliary tubercles. There are tuberculous caseous tracheobronchial lymph nodes.

lung with marked bronchiectasis (fig. 12). Bronchiectasis was suggested clinically by the persistent cough, which at times was paroxysmal. The anatomic examination (fig. 13) confirmed the clinical and roentgenographic interpretation. In addition, necropsy revealed a cavity in the periphery of the right lung which was not diagnosed by physical examination and was not suggested by the roentgenograms. The cavity may have been filled with secretion when the examinations were made. There was more extensive tuberculosis in the left lung than was sug-

gested by the roentgenogram. Disseminated tubercles and moderately enlarged tracheobronchial lymph nodes were found at necropsy, but were not suggested by the roentgenograms.

GROUP II[2]: THREE CASES OF PULMONARY TUBERCULOSIS WITHOUT CAVITY FORMATION AND (FOR COMPARISON) A CASE OF CHRONIC NONTUBERCULOUS PNEUMONIA IN A TUBERCULOUS CHILD

In two of these children (cases 7 and 8) there was clinical and roentgenographic evidence of pulmonary tuberculosis, which was confirmed by postmortem examination. In the third (case 9) there was neither clinical nor roentgenographic evidence of the extensive pulmonary tuberculosis found at necropsy. In the fourth (case 10), interstitial pneumonia occurring in a tuberculous child presented a picture difficult to differentiate clinically and roentgenographically from pulmonary tuberculosis.

CASE 7.—*Tuberculous mesenteric, retroperitoneal and tracheobronchial lymphadenitis; caseous tuberculous pneumonia; disseminated miliary tubercles in the viscera; tuberculous meningitis.*

History.—F. W., a boy, was admitted to the hospital at the age of 16 months; death occurred five days later. There was a boarder with tuberculosis in the home when the patient was from 4 to 8 months of age. He had intimate contact with three siblings who had "abscesses in the neck" in infancy.

The patient was born in October, 1921. He was breast-fed until two weeks before admission; he had received complementary food since 7 months of age; the feeding was irregular. He took a prize at a baby show in October, 1922.

Early in December, 1922, the child had "bronchitis" with cough and fever, which improved; but the last of December be became feeble and weak, with frequent vomiting and loss of appetite. Then slight improvement seemed to occur, but in the second week of January he had fever which had been constant for the past five weeks; restlessness, pallor, loss of weight and slight edema of the extremities had been present for two weeks.

The patient was in the hospital from Feb. 23 to 27, 1923 (five days).

Examination on Admission.—The weight was 8,480 Gm. The patient was an acutely and chronically ill child; he was toxic and pale, breathed with an expiratory grunt, and had a loose, dry skin (tuberculids?). The right ear drum was red and bulging; the left drum was dull, gray and slightly bulging; the pharynx was red. The chest was hyperresonant; the left side was fuller than the right, with impairment at the bases of both lungs; râles were present; from the apex of the right lung to the angle of the right scapula dulness and a suggestion of amphoric breath sounds were noted. The spleen and liver were large and hard.

Clinical Course.—The temperature was elevated, rising each day to between 38.4 and 39.4 C. (101.5 and 102.8 F.). There was a gradual failure, with development of tremor of the upper extremities. On the third day, hyperesthesia and irritability were present; the knee reflexes were exaggerated; the Kernig sign was negative; there was no stiffness of the neck. The lungs were as before, with dulness and diminished breath sounds on the right.

Laboratory Data.—The reaction to 0.1 mg. of tuberculin was negative. The white blood cells numbered 17,000, with 96 per cent polymorphonuclears. On Feb. 26, 1923, the spinal fluid contained 60 cells; the reaction for globulin was 2 plus. The sputum was negative for tubercle bacilli.

Roentgen Observations.—Roentgenograms taken on Feb. 24 and 26, 1923, were similar. That taken on February 26 (fig. 14), the day before death, showed well marked mottled shadows more dense and confluent in the upper and middle lobes of the right lung.

Postmortem Examination (Complete).—The lungs showed disseminated miliary (acute) tubercles (fewer in the left than in the right), tuberculous pneumonia, the entire right lung being consolidated, and a caseous mass in the middle lobe

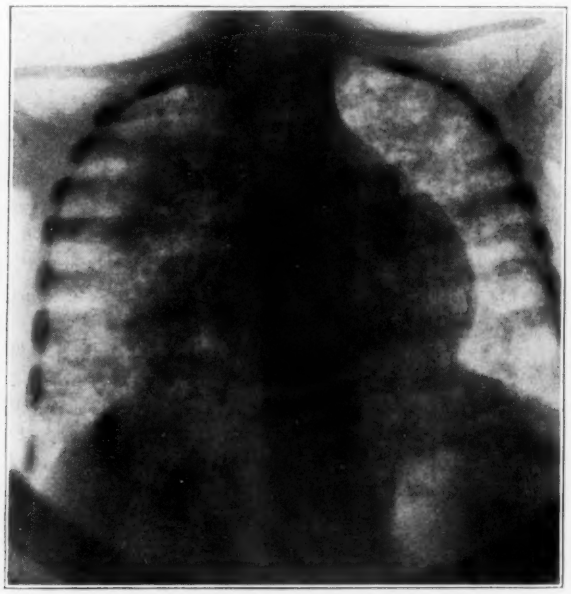


Fig. 14 (case 7).—Roentgenogram taken on Feb. 26, 1923, the day before death. There are bilateral generalized mottled shadows with large confluent areas in the upper and middle lobes of the right lung. (This photograph is a contact print of the roentgenogram. The light and dark shadows are reversed.)

of the right lung, 2.5 cm. in diameter. There was no bronchitis. The pleurae were normal. The peritracheal lymph nodes (fig. 15) were 4 by 3 by 2.5 cm. in diameter, caseous and necrotic; there was bilateral peribronchial tuberculous lymphadenitis, with retroperitoneal and mesenteric caseous lymphadenitis. Disseminated miliary tubercles were found in the viscera. Tuberculous meningitis was present.

Bacteriology.—Histologic sections of the lungs showed tubercle bacilli. The peritoneal fluid contained Staphylococcus aureus.

Comment.—Whether the "bronchitis" which had occurred two months before admission had been an acute nontuberculous pulmonary

infection or was the beginning of the tuberculous pneumonia that later caused death it is impossible to state positively, but the latter explanation is probable. The roentgenogram taken the day before death (fig. 14) showed extensive generalized mottling over both lungs with some larger areas of increased density, particularly on the right. It suggested an extensive pulmonary infection with disseminated areas of pneumonia, presumably of tuberculous origin. At necropsy there were found disseminated tubercles, less extensive than intimated by the roentgenogram, and consolidation of the entire right lung with focal caseation. These findings were not exactly what would have been expected

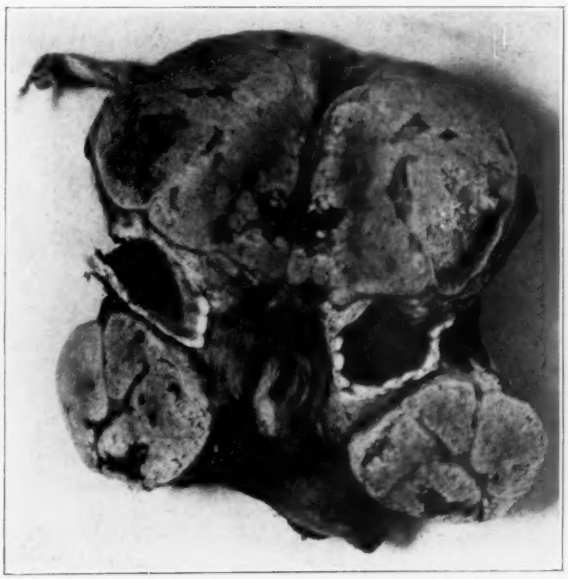


Fig. 15 (case 7).—The peritracheal lymph nodes.

from the roentgenogram. A photograph is shown of the large peritracheal glandular mass (fig. 15), which could not be identified by any circumscribed shadow in the roentgenogram.

As is sometimes the case with acute fulminating tuberculosis, particularly in the presence of tuberculous meningitis, the reaction to tuberculin in this child was negative. If his stay in the hospital had been longer and an injection of old tuberculin stronger than 0.1 mg. had been given, there might have been a positive reaction. In spite of the negative reaction to tuberculin, the diagnosis of tuberculosis was made, not so much from any characteristics of the roentgenogram as from the history, the physical examination and the clinical course of the disease.

CASE 8.—*Tuberculous mesenteric, peribronchial and cervical lymphadenitis; pulmonary tuberculosis with fibrinous pleurisy (apex of the right lung); ulcerative tuberculous tonsillitis and laryngitis; ulcerative tuberculous enteritis; disseminated tubercles in the viscera.*

History.—V. M., a girl, was admitted to the hospital at the age of 2½ months; the age at death was 6 months. The tuberculous contact was not known.

The patient was born on Oct. 5, 1924. The weight at birth was 6 pounds and 14 ounces (3 Kg.). She was breast-fed for one month; thereafter, she was given irregular inadequate feedings of unpasteurized milk part of the time and of proprietary foods. She had "colic" and constipation constantly.

The patient was in the hospital from Dec. 29, 1924, to April 10, 1925 (three and one-half months).

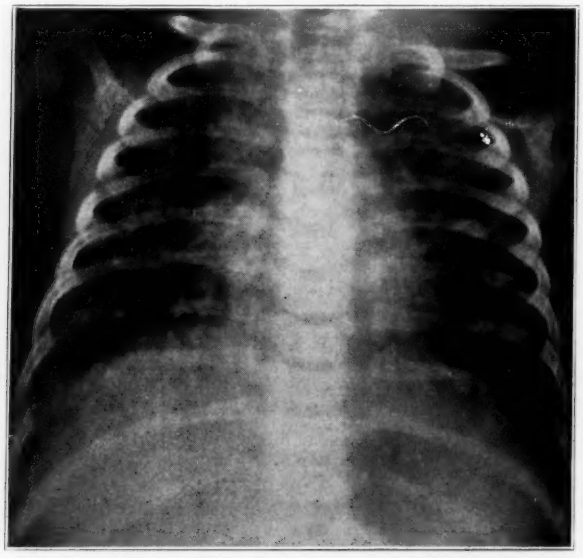


Fig. 16 (case 8).—Roentgenogram taken on March 23, 1925, eighteen days before death. There is bilateral generalized mottling with a circumscribed area of greater though not homogeneous density in the right upper inner zone.

Examination on Admission.—The patient was a sallow, pasty-looking child, who was moderately undernourished. There were edema of the face and feet, catarrhal otitis media and mild pharyngitis. The lungs were clear.

Clinical Course.—On admission the weight was 3.25 Kg.; there was no gain during the stay in the hospital. Fever was continuous, frequently rising to 39 and 40 C. (102.2 and 104 F.). The appetite was poor; there was an increase in dystrophy and weakness. Bilateral purulent otitis media was present. Bilateral cervical lymphadenitis with incision resulted in a draining sinus on the left; a purulent abscess over the left clavicle was incised. The right lung showed slight changes on January 31, which gradually increased. On April 7, there were difficult respiration, retraction of the lower part of the sternum and dulness in the upper lobe of the right lung and in the right axilla and interscapular region; the breath sounds were tubular, with fine râles; the left lung was hyperresonant to percussion, with diminished breath sounds over the upper lobe.

Laboratory Data.—The reaction to 0.1 mg. of tuberculin was negative on December 29; it was positive to 1 mg. on February 1. On admission, the red blood cells numbered 3,136,000; the white blood cells, 10,400, with 33 per cent polymorphonuclears. On April 5, the sputum was positive for tubercle bacilli. On April 10, the spinal fluid contained 28 cells; the Pandy reaction was faintly positive. A culture of the exudate from the abscess of the neck showed Streptococcus nonhaemolyticus; that of the exudate from the right cervical lymph node, Streptococcus haemolyticus, and that of the exudate from the left cervical lymph node, Streptococcus haemolyticus.

Roentgen Observations.—Roentgenograms were taken on Feb. 5, 12, 19 and 26, March 13 and 23 and April 7, 1925. The first film showed faint bilateral disseminated "miliary" shadows and a faint haziness of the right lung, with a defi-

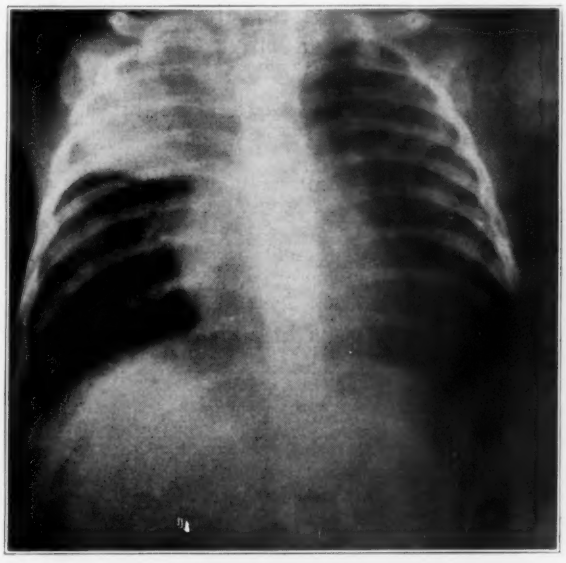


Fig. 17 (case 8).—Roentgenogram taken on April 7, 1925, three days before death. (It is slightly out of focus.) There is bilateral generalized mottling. The upper lobe of the right lung is demarcated by a dense homogeneous shadow.

nite shadow in the inner zone of the upper lobe. Throughout the series the "miliary" shadows became more marked, and the shadow in the upper lobe of the right lung became more sharply outlined, as seen in the film taken on March 23 (fig. 16), eighteen days before death. The film taken on April 7 (fig. 17), three days before death, showed a heavy, homogeneous, clearly demarcated shadow in the upper lobe of the right lung.

Postmortem Examination (Complete).—The lungs showed proliferative tuberculosis, which was extensive in the upper lobe of the right lung, but also involved the middle and lower lobes and the upper lobe of the left lung. There was fibrinous pleurisy at the apex of the right lung. There was bilateral peribronchial tuberculous lymphadenitis; the lymph node on the right measured 3 by 1 by 6 cm.; the node on the left was smaller. There were tuberculous cervical and mesenteric lymphadenitis, tuberculous ulcerative tonsillitis and laryngitis and

tuberculous ulcerative enteritis. Disseminated tubercles were present in the viscera and in the brain.

Bacteriology.—B. tuberculosis was recovered from all of the involved organs (histologically).

Comment.—It is interesting that of the last two films taken and here reproduced, that of March 23 (fig. 16), eighteen days before death, seemed to express more exactly the condition of the lungs as found at necropsy than the one taken three days before death, April 7 (fig. 17). At the time of the latter there was clinical evidence of an acute process in the upper lobe of the right lung; this was confirmed by the roentgenogram. But three days later, at necropsy, no lesion was found which conceivably could have given the smooth, homogeneous, clearly outlined shadow shown in the upper lobe of the right lung in the film taken on April 7 (fig. 17). A possible explanation seems to be that in the interim of three days (between the time this film was taken and the time of death) the process—whether caused by exudation or atelectasis—had a chance to clear, so that at the time of death there remained only the underlying extensive chronic condition which the film taken on March 23 (fig. 16) showed. In this earlier film (fig. 16), the generalized coarse mottling, with an area of denser shadow in the right upper inner zone, suggested tuberculosis, particularly as it occurred in a child with a positive reaction to tuberculin and having other clinical features of tuberculosis. The shadow in the upper lobe of the right lung was presumably of parenchymal origin; for, in the necropsy report, the tracheal lymph nodes were not mentioned, and the shadow was probably too high in the chest to have been caused by the large peribronchial mass of lymph nodes. The shadow also does not seem to be sufficiently homogeneous for a glandular mass.

CASE 9.—*Tuberculous peribronchial lymphadenitis; pulmonary tuberculosis and tuberculous pleurisy; tuberculous meningitis.*

History.—D. M., a girl, was admitted to the hospital at the age of 6¾ years; death occurred ten days later. An older sister had been ill with tuberculosis and several years previously was at a sanatorium. Raw milk was used.

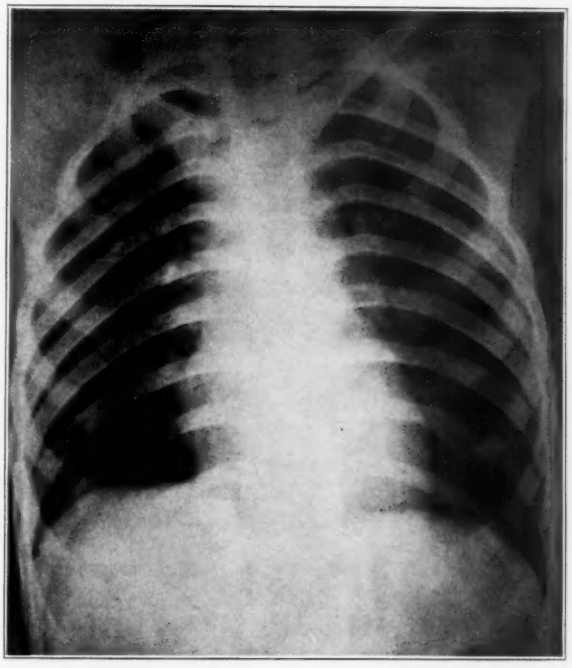
The patient was born on Feb. 5, 1920. She was breast-fed for two months. She had measles one year prior to examination and whooping cough the previous summer; she had frequent colds.

On Oct. 25, 1926, sixteen days before admission, the child had a fall with resulting pain over the left eye, thick speech, vomiting and two convulsions. She became comatose and cyanotic, but recovered. Three days later, she vomited three or four times. Three days later, she had pain in the left leg, with prickly pains in the leg and hands and twitching of the face and head. The symptoms were repeated the next day. There was increasing restlessness, with twitchings and drowsiness. On the tenth day of illness she was taken to Waterbury Hospital for five days. The temperature varied from 101.6 to 102.6 F.; the pulse rate, from 60 to 80. The white blood cells numbered 26,000 with 85 per cent polymorpho-

nuclears. The spinal fluid contained 35 cells; it was under increased pressure, and contained a trace of globulin.

The patient was in the hospital from Nov. 10 to 19, 1926 (nine days).

Examination on Admission.—The patient was a thin, sick, irritable child; she was drowsy, complained of pains in the neck and lay on her side. The lungs were clear. The left optic disk was blurred.



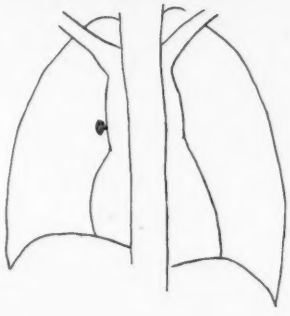


Fig. 18 (case 9).—Roentgenogram taken on Nov. 18, 1926, the day before death. The chest is in inspiration, with slight rotation to the right. In the right side of the chest the apex and periphery are slightly hazy; there is slight accentuation of the trunk markings. The mediastinum is slightly increased in width. There is a small circumscribed dense area overlying the sixth rib near the articulation (calcium).

Clinical Course.—There was fever, generally swinging from 38 to 39 C. (100.4 to 102.2 F.), with a terminal rise to 41.4 C. (106.5 F.). The course was steadily downhill; the patient was delirious and comatose. On the second day stiffness of the neck, left internal strabismus, left facial weakness and choked disk developed. On the sixth day she had convulsions and opisthotonos. On the eighth day, there was ptosis of the left eyelid; the chest was filled with loud coarse râles; respiration was very shallow, and cyanosis was present.

Laboratory Data.—The reaction to 0.1 mg. of tuberculin was positive. On November 10, the spinal fluid was cloudy and under increased pressure, it contained 400 cells, with 92 per cent lymphocytes; the Pandy test showed a trace of globulin; there was a flocculent precipitation in four hours. On November 11, the spinal fluid was cloudy and under increased pressure; it contained 360 cells; the Pandy test showed a trace of globulin; a film formed; tubercle bacilli were present.

Fig. 19 (case 9).—The right lung, showing generalized and focal pulmonary tuberculosis and pleural fibrous adhesions.

Roentgen Observations.—Roentgenograms were taken on Nov. 12, 16, 17 and 18, 1926. They all resembled that taken on November 18 (fig. 18), the day before death, in that they showed a moderate increase of normal pulmonary shadows and slight generalized mottling. The mediastinum was slightly wider than normal. In the right hilar region was a shadow indicating a calcified lymph node.

Postmortem Examination (Complete) (fig. 19).—There was chronic bilateral proliferative and acute exudative pulmonary tuberculosis; it was more marked

on the right than on the left. Calcified zones were noted in the apex and at the hilus of the right lung. There were pleural adhesions on the right; in addition, bilateral fibrinous pleurisy was present. Bilateral tuberculous peribronchial lymphadenitis with caseation and calcification was present. Tuberculous meningitis was noted.

Bacteriology.—Tubercle bacilli were recovered from the lymph nodes on direct smear and inoculation into a guinea-pig.

Comment.—The roentgenograms of this child have been most difficult to interpret because of the impossibility of correlating their comparative clarity with the extensive pulmonary involvement found at necropsy (fig. 19). The pertinent question of the identification of the roentgenograms has been investigated. There was at that time no other patient of the same name in the hospital; four roentgenograms were taken on four different dates, and the name and number appeared on them all and agreed with those of the roentgenographic reports attached to the history; there were notes on the clinical chart to the effect that at least on two of the dates the child was taken to the roentgenographic laboratory; the appearance of the four roentgenograms was similar and answered the description of them in the reports attached to the history. At the end of the protocol of the necropsy there was the statement: "N. B.: It is of interest to note that during the entire stay in the hospital the physical and x-ray findings of the chest never suggested the findings of the autopsy."

Aside from whooping cough the summer before and frequent infections of the upper respiratory tract, the child had had no pulmonary symptoms prior to admission. During the stay in the hospital attention had been focused entirely on the meningeal signs and symptoms; little attention had been given to examination of the chest, but note had been made that examination was difficult owing to shallow, slow respirations, and on the last day of life, loud, coarse râles were heard. The four roentgenograms taken during her ten day stay in the hospital were all similar in appearance. The last one, taken on November 18 (fig. 18), the day before death, was of softer quality than the others and showed a slight haziness at the apex and periphery of the right lung and a slight accentuation of the pulmonary markings, as often associated with an infection of the upper respiratory tract as with pulmonary disease. Because the chest was well expanded in inspiration it hardly seemed possible that the wide mediastinal shadow could have been caused by the moderate tracheobronchial lymphadenitis found at autopsy. There was in the right hilus the shadow of calcium in a lymph node. It is impossible to explain why the extensive tuberculous lesions of the parenchyma of the lungs should have given no comparable roentgenographic evidence. This case illustrated the limitations of the roentgenogram.

CASE 10.—*Tuberculous mesenteric lymphadenitis, otitis media and mastoiditis; disseminated tubercles in the spleen; nontuberculous interstitial pneumonia.*

History.—C. L., a boy, was admitted to the hospital at the age of 10 months; the age at death was 16 months. The tuberculous contact was not known.

The patient was born on Dec. 27, 1921. The weight at birth was 8¼ pounds (3.7 Kg.). He was breast-fed for one month; feeding was difficult, and he vomited. He failed to gain well. He had recurrent attacks of otitis media; it was bilateral at the age of 2 months and lasted for one month; it occurred on the left at 6 months and lasted one week; it was bilateral and persistent from 9 months until the time of admission. There had been right preauricular swelling for the past two weeks. The patient was seen in the New Haven Dispensary on Oct. 25, 1922, and hospitalization was advised.

The patient was in the hospital from Nov. 6, 1922, to April 30, 1923 (five and three-quarter months).

Fig. 20 (case 10).—Roentgenogram taken on April 24, 1923, six days before death. The chest is in expiration. There are bilateral diffuse dense mottled shadows which are more marked on the right. The bases and periphery are clear.

Examination on Admission.—The patient was sick and in pain; he was malnourished. There were partial paralysis of the right side of the face, bilateral purulent otitis media, with preauricular swelling, and furunculosis. The lungs were clear.

Clinical Course.—On admission the weight was 5.6 Kg. There was no gain during the stay in the hospital. The patient had irregular fever, usually around 38 C. (100.4 F.), with occasional higher elevations. The appetite was variable. There was continued furunculosis requiring incision. Bilateral purulent otitis media occurred, for which repeated paracentesis was carried out. (Histologically, granulation tissue from the right ear appeared to be tuberculous, but there were no demonstrable tubercle bacilli. A guinea-pig inoculated with pus died of intercurrent infection.) There was right preauricular lymphadenitis. Bilateral mastoidectomy was performed; healing occurred, but with discharging sinuses. There were persistent facial paralysis on the right and continued cough. The signs in the lungs were at first minimal and gradually increased; they were always more

marked over the upper lobes, with dulness especially in the right interscapular region. On April 25, the upper lobe of the right lung was dull, with bronchial breath sounds; that of the left lung was similar; these were large, moist crepitant râles. On April 29, the right lung was flat to percussion, and there were tubular breath sounds; the same changes were noted in the upper lobe of the left lung. There were transient neurologic abnormalities in the eyes and reflex reactions, with increased muscular twitching. Terminal edema developed with urinary findings of albumin, casts and cells.

Laboratory Data.—The reaction to 0.02 mg. of tuberculin was "strongly positive." On November 11 and 12 and February 11, the sputum was negative for

Fig. 21 (case 10).—Photomicrograph of the lung, showing interstitial pneumonia. Hematoxylin and eosin stain; × 70.

tubercle bacilli. On February 6 and 11, the spinal fluid contained 2 and 0 cells, respectively; the reaction for globulin was negative. On admission, the white blood cells numbered 11,000, with 57 per cent polymorphonuclears; there was little change subsequently.

Roentgen Observations.—Fifteen roentgenograms were taken between Nov. 8, 1922, and April 24, 1923 (fig. 20). The first film showed a small shadow in the inner zone of the upper lobe of the right lung. This increased downward and outward. After three months a faint shadow appeared in the inner zone of the upper lobe of the left lung and gradually increased in extent. These shadows were always mottled and had no circumscribed outline. The film taken on April 24 (fig. 20), one week before death, still showed the bases and peripheries

of the lungs clear; elsewhere there was a diffuse mottled shadow which suggested strongly in places the "snow-flake" appearance of miliary tuberculosis.

Postmortem Examination (Partial) (fig. 21).—There was interstitial pneumonia (nontuberculous) involving both lungs, but more extensive in the right; the lower lobe of the left lung was normal. The tracheobronchial lymph nodes were uninvolved. Tuberculous caseous and calcified mesenteric lymphadenitis and tuberculous mastoiditis and otitis media were present. There were tubercles in the spleen.

Bacteriology.—Spirochetes and tubercle bacilli were not found (histologically).

Comment.—In this case a series of fifteen roentgenograms was taken over a period of five and one-half months, and the pictures showed the gradual development of extensive shadows in both lungs. These shadows always had a fluffy, mottled appearance with hazy borders and were more dense in the inner zone. The bases and periphery of the lungs were notably clear. The film here reproduced (fig. 20) was taken one week before death. Because of the nature of the pulmonary signs, the appearance of the roentgenographic shadows of the lungs, the known presence of a tuberculous infection and probable tuberculous otitis media, the pulmonary condition was considered without a doubt to be tuberculosis. After the postmortem observation of nontuberculous interstitial pneumonia (fig. 21) and of nontuberculous tracheobronchial lymph nodes, the films were reexamined. The generalized bilateral fluffy mottling certainly had the appearance usually thought to be fairly characteristic of tuberculous pneumonia, but such an extensive tuberculous process would probably have involved the bases and periphery to a greater degree and the shadow in the mesial region would have been more homogeneous.

GROUP III: FOUR CASES OF TUBERCULOSIS IN WHICH TRACHEOBRONCHIAL LYMPHADENITIS WAS THE OUTSTANDING FEATURE

In two of these cases the roentgenograms gave a clear outline of the enlarged lymph nodes which were found at necropsy (cases 11 and 12). Shadows of the lymph nodes were not visible in the roentgenograms of the other two. In one of these cases (case 13) the presence of enlarged nodes could be inferred from the evidence of bronchial compression; in the other case (case 14) there was no roentgenographic evidence of tracheobronchial lymphadenitis, but at necropsy it was found that a caseous lymph node had ruptured into the bronchus.

CASE 11.—*Tuberculous mesenteric, retroperitoneal, tracheobronchial and cervical lymphadenitis; compression of the left bronchus; disseminated visceral tuberculosis; disseminated tubercles in both lungs; pleural adhesions (left); focal pneumonia.*

History.—N. J., a boy, was admitted to the hospital at the age of 7½ months; the age at death was 15 months. "Sometime before admission" the patient visited a maternal aunt in New York State, who had tuberculosis and who was in a sanatorium for tuberculosis at the time of the child's admission to the hospital.

The patient was born on Aug. 19, 1922. The weight at birth was 8½ pounds (3.8 Kg.). He was breast-fed to the time of admission. The Wassermann reaction was 4 plus. He was given irregular treatment with mercury inunctions. Cough and fever were present for one month, and furunculosis for ten days.

The patient was in the hospital from April 3 to Nov. 16, 1923 (seven and a half months).

Examination on Admission.—The patient was a well nourished but sick-looking colored baby; he coughed occasionally. There were a few pustules on the chest, abdomen and scalp, and crusted and purulent red ulcers with a clean periphery on the buttocks. The ear drums were dull; the pharynx was red, and the tonsils were large. The upper lobe of the left lung showed diminished resonance, with diminished voice and breath sounds.

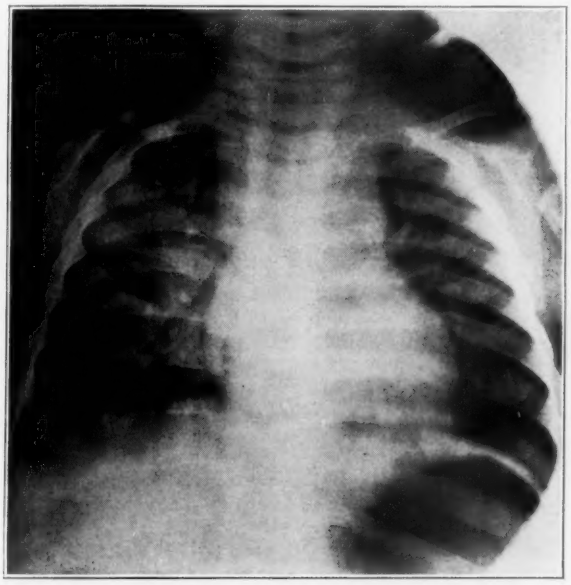


Fig. 22 (case 11).—Roentgenogram taken on Nov. 9, 1923, one week before death. The chest is in partial expiration. In the right side of the chest, the upper lobe shows a generalized but not homogeneous shadow, which is more dense near the clearly demarcated interlobar septum; the middle and lower lobes show an irregular shadow in the inner and middle area. The left side of the chest is slightly hazy. The mediastinum is uniformly increased in width. The right bronchial markings are accentuated.

Clinical Course.—On admission the weight was 6.8 Kg.; there was practically no gain during the patient's stay in the hospital. The temperature was always more or less elevated. Stubborn and persistent furunculosis was present throughout the course (proved to be nontuberculous by biopsy on April 5, 1923, and at necropsy). Chronic purulent otitis media was present. The lungs showed signs of diminished or suppressed breath sounds, with dulness always more or less on the left and marked over the upper lobe of the left lung. On April 30, flatness was noted at the base of the left lung. On May 2, thoracentesis was performed;

1 cc. of fluid was obtained with white and red blood cells; "no growth" was obtained. On July 29, there was a sudden onset of rapid respiration, with an asthmatic stridor and wheezes, cough, cyanosis and abdominal distention. These symptoms gradually diminished during the next month. On August 4, the apex of the right lung was dull to percussion, with harsh breath sounds and fine râles.

Fig. 23 (case 11).—The larynx, trachea and lungs, with the lymph nodes. There are large caseous cervical, peritracheal and peribronchial lymph nodes. The right lung shows bronchopneumonia and ulcerative tuberculous bronchitis. Both lungs show disseminated tubercles. The left pleura shows fibrous adhesions.

On November 7, scarlet fever developed, with marked cervical adenitis and signs of pneumonia at the bases of both lungs. Treatment was symptomatic; five antisyphilitic treatments with mercury inunctions and neoarsphenamine were given; exposure to sunlight was given.

Laboratory Data.—The reaction to 0.02 mg. of tuberculin was "strongly positive." On admission, the white blood cells numbered 14,500 with 67 per cent polymorphonuclears.

Roentgen Observations.—Eleven roentgenograms were taken between April 4, and Nov. 9, 1923. The reports of all films noted the marked width of the mediastinal shadow. In the upper lobe of the right lung in most of the films there was a more or less definite shadow. The film taken on November 9 (fig. 22), one week before death, demonstrated the same shadow and confluent shadows in the lower part of the upper lobe and in the middle lobe of the right lung. In addition there were mottled shadows in both lungs, particularly the right along the interlobar fissure and along the bronchi, the outlines of which were accentuated.

Postmortem Examination (Partial) (fig. 23).—The left lung showed diffusely disseminated tubercles. The right lung showed acute bronchopneumonia, chiefly in the upper lobe; in this lobe, there were diffusely disseminated tubercles and in the middle and lower lobes, a few tubercles. There was ulcerative tuberculous bronchitis. The left pleura showed fibrous adhesions involving the entire cavity; the right pleura was uninvolved. Tuberculous tracheobronchial lymphadenitis was present; there was a mass of nodes around the left bronchus 5 cm. in diameter, compressing it considerably but not completely; there were nodes also around the aorta and the pulmonary vessels, but there was no encroachment to cause compression. Tuberculous cervical, mesenteric and retroperitoneal lymphadenitis was present. Disseminated tubercles were found in the liver. The lesions of the skin were nontuberculous, healing furuncles.

Comment.—The most noteworthy feature of the roentgenogram (fig. 22) was the wide mediastinal shadow (an appearance which was present in all of the series of eleven roentgenograms). There were clinical signs and symptoms such as are usually caused by abnormal mediastinal pressure; there was found at necropsy a large mass of lymph nodes in this region, confirming the diagnosis of tracheobronchial lymphadenitis.

The persistence through seven months of a shadow in the upper lobe of the right lung accompanied by physical signs of tracheobronchial lymphadenitis, occurring in a boy with a positive reaction to tuberculin, would point to tuberculosis as the cause of the pulmonary shadow. The film taken one week before death (fig. 22), at which time the child had scarlet fever, showed evidence of acute bronchopneumonia. The appearance of the dilated bronchi within the shadows in the lower lobe of the right lung suggested a diagnosis of ulcerative bronchitis—presumably tuberculous in this case—which was confirmed at necropsy.

Although there was acute suppurative cervical lymphadenitis accompanying the scarlet fever, it was evidently superimposed on an old caseous, tuberculous process in these nodes.

CASE 12.—*Tuberculous mesenteric and bronchial (left) lymphadenitis; tuberculous ulcerative colitis; chronic tuberculous peritonitis; disseminated tubercles in the liver and lungs.*

History.—R. B., a boy, was admitted to the hospital at the age of 14¾ years; death occurred six weeks later. The tuberculous contact was not known.

The patient was born on June 17, 1913. He had had measles and whooping cough. He had always had abdominal distention and diarrhea.

For one week he had had epigastric discomfort, had vomited twice and had had three loose stools a day.

He was in the hospital from March 3 to April 30, 1928 (six weeks).

Examination on Admission.—The weight was 98 pounds (44.5 Kg.). Nutrition was poor. The lungs were clear except for a relative dulness at the bases, more on the right than on the left. The abdomen was distended, with dulness in the flanks.

Clinical Course.—There were no pulmonary symptoms or signs. On March 31, laparotomy was performed: "peritoneum thick, bowel adherent to peritoneum. Small opening of bowel repaired." There was infection of the abdominal wound with a fecal fistula. The course was downhill.

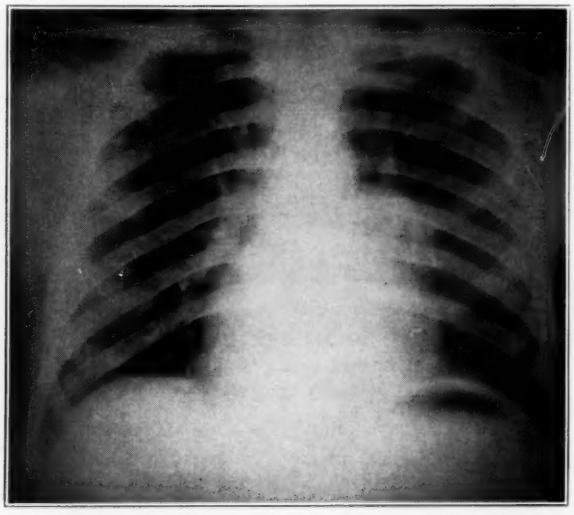


Fig. 24 (case 12).—Roentgenogram taken on March 21, 1928, six weeks before death. There is a homogeneous circumscribed shadow in the left hilar region.

Laboratory Data.—The reaction to 0.02 mg. of tuberculin was positive. The white blood cells numbered 13,000, with 84 per cent polymorphonuclears. Biopsy of the peritoneum showed: "chronic peritonitis, probably tuberculous."

Roentgen Observations.—A roentgenogram taken on March 21, 1928 (fig. 24), was clear, except for marked circumscribed enlargement of the left hilar shadow. The abdomen was normal.

Postmortem Examination (Partial).—The lungs showed disseminated tubercles; the pleurae, fibrous pleural adhesions, and the lymph nodes, tuberculous tracheobronchial lymphadenitis. Acute and chronic tuberculous peritonitis was found. There were disseminated tubercles in the liver. Tuberculous mesenteric lymphadenitis was present.

Comment.—Although this boy never had pulmonary signs or symptoms, he is included in this series because his roentgenogram showed a circumscribed shadow extending outward from the left hilar

region. This shadow is of the type about which there is frequent discussion as to whether it is caused by abnormal pulmonary or lymphoid tissue. The definiteness of outline and homogeneity of the shadow in this instance should suggest a diagnosis of enlargement of the lymph nodes as pointed out by Le Marc'hadour, Dupire and Loé.[5] At necropsy there were found minute disseminated tubercles throughout the lungs (and liver) and a large mass of tuberculous lymph nodes in the left hilus, a number of which were 2 cm. or more in diameter. There may have been some compression of the parenchymal tissue in this zone to cause the large shadow in the roentgenogram, but it seems remarkable that extensive tuberculous involvement of the pulmonary tissue and atelectasis were not found.

CASE 13. —*Tuberculous mesenteric and tracheobronchial lymphadenitis with compression of the left bronchus; pulmonary emphysema (left); tuberculous pneumonia; costophrenic pleurisy; disseminated miliary tuberculosis.*

History.—F. D., a girl, was admitted to Waterbury Hospital[6] at the age of 5 months; death occurred six days later. The mother died of pulmonary tuberculosis at Waterbury Hospital on Oct. 30, 1930. The history was uncertain as to direct contact of the patient with her mother.

The patient was born on June 17, 1930. She was never breast-fed. She was "always well."

The patient had a "cold" for two weeks prior to admission. Three days before admission the cold became worse, and there was a loose cough. There was constant vomiting. One day before admission, she had difficulty of respiration.

She was in the hospital from Nov. 16 to 21, 1930 (six days).

Examination on Admission.—Nutrition and development were poor. The weight was 14 pounds (?) (6.4 Kg). There was slight continuous cyanosis, which increased with crying. There was a purulent nasal discharge; the left ear drum was red; the pharynx was red and boggy. The right lung showed more expansion than the left, but was dull to percussion throughout, especially at the upper third, front and back. The breath sounds were bronchovesicular and exaggerated, with a few coarse and medium moist râles. The left lung was hyperresonant; breath sounds were absent throughout. The heart was displaced to the right so that the left border coincided with the left sternal margin; the sounds were of good quality. The pulse was rapid. The spleen and liver were not palpable, and no masses or spasm was noted. The reflexes were not abnormal.

Clinical Course.—There was obstinate vomiting, although the patient was somewhat relieved by the administration of an alkaline dextrose solution. An oxygen tent was used. A subcutaneous injection of saline solution, an intravenous injection of dextrose solution and a transfusion were given.

Laboratory Data.—The reaction to 0.01 mg. of tuberculin was 4 plus. Examination of the blood (before transfusion) showed: red cells, 3,100,000; white cells, 12,300, with 55 per cent polymorphonuclears and 38 per cent lymphocytes.

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5. Le Marc'hadour, A.; Dupire, P., and Loé, R.: Tracheobronchial Adenopathy in Children: Clinical and Roentgenologic Aspects, Paris méd. **2**:441 (Nov. 28) 1931.

6. Dr. J. Harold Root and Dr. Joseph L. Hetzel allowed us to report this case.

Roentgen Observations.— A roentgenogram taken on November 17, four days before death (fig. 25), showed: "emphysema of left lung with moderately diffuse infiltration through both lungs. Left diaphragm depressed and mediastinum pushed to right displacing the heart." Fluoroscopic examination showed: "Motion of right diaphragm increased; that of left very slight. When right diaphragm descends, left rises just a trifle and vice versa. Mediastinum moves to right as the right diaphragm descends and left diaphragm rises slightly, i. e., on inspiration. The lateral motion is not more than an inch. Diagnosis: ball-valve obstruction of lung with scattered pulmonary tuberculosis in both lungs."

Postmortem Examination (fig. 26).—The right lung showed focal tuberculous pneumonia with little emphysema; the left lung, marked emphysema with slight focal caseous tuberculous pneumonia. There was slight costophrenic pleurisy.

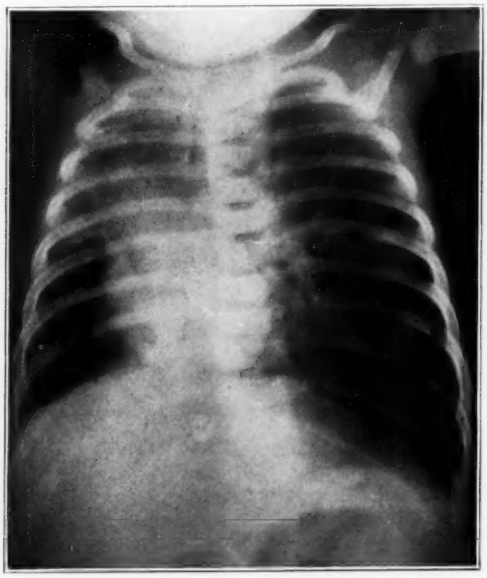

Fig. 25 (case 13).—Roentgenogram taken on Nov. 17, 1930, four days before death. The heart and trachea are markedly displaced to the right. The left lung is overaerated (emphysema); the upper lobe is somewhat hazy. There is a dense shadow in the upper lobe of the right lung.

The lymph nodes showed peribronchial and peritracheal caseous tuberculous lymphadenitis with partial compression of the left bronchus by adhesions and a collar of nodes, each the size of a pea or a kidney bean. The mesenteric nodes were swollen and congested but not caseous. There were miliary tubercles in the liver, spleen and peritoneum.

Comment.—The appearance of the roentgenogram (fig. 25) indicated that there was a pathologic process in the right upper zone with compensatory emphysema elsewhere particularly throughout the left lung, so that the heart and mediastinal contents were displaced to the right. Physical examination supported the diagnosis of the presence

of such a lesion. There was no history of inhalation of a foreign body, but there had been a probable intimate tuberculous contact; the child gave a positive reaction to tuberculin, and a presumptive diagnosis was made of pulmonary tuberculosis, with emphysema of the left lung due to partial occlusion of the left main bronchus by the pressure of tuberculous lymph nodes. The roentgenogram revealed no shadows indicative of these lymph nodes, and at necropsy they were found to be small (fig. 26, from drawing by Dr. J. L. Hetzel). Their importance was due to their anatomic position adherent to and encircling the bronchus, compressing it and causing the signs and symptoms of a ball-valve occlusion.

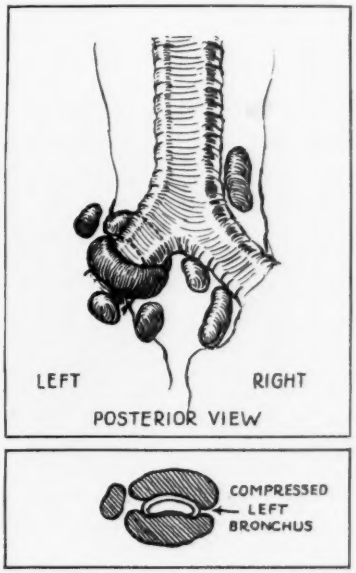

Fig. 26 (case 13).—The tracheobronchial lymph nodes.

It is interesting to contrast these rather small lymph nodes, which gave such marked symptoms, with the mass of lymph nodes in case 12, which was clinically unrecognized.

CASE 14.—*Tuberculous bronchial lymphadenitis with rupture into the left bronchus; acute and chronic pulmonary tuberculosis; tuberculous ulcerative bronchitis; disseminated miliary tubercles in the viscera.*

History.—B. B., a boy, was admitted to the hospital at the age of 19¾ months; death occurred two days later. The mother had moderately advanced pulmonary tuberculosis. She died later, in July, 1927.

The patient was born on Sept. 3, 1924. He was breast-fed for one year. He was seen frequently in New Haven Dispensary from November, 1924, to June, 1925, for mild infections and acute rickets; the weight increased from 4.2 to 8 Kg.

The patient had measles about April 1, 1926, with residual fever, cough and a poor appetite. On April 15, in New Haven Dispensary, a diagnosis of "unresolved

pneumonia" in the upper lobe of the left lung, bilateral catarrhal otitis media and pharyngitis was made. The spleen was palpable. Anemia was present.

The patient was in the hospital from April 26 to 28, 1926 (two days).

Examination on Admission.—The child was very ill, irritable, pale and cyanotic; dehydration was present; respiration was rapid. There were a fading measles rash and tuberculids. The pharynx was red; bilateral catarrhal otitis media was present. The spleen and liver were enlarged. The lungs showed poor

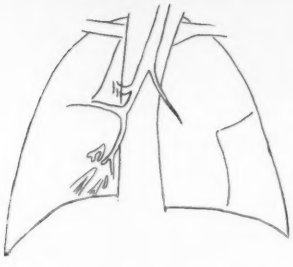

Fig. 27 (case 14).—Roentgenogram taken on April 26, 1926, two days before death. In the left side of the chest, the upper lobe shows a dense homogeneous shadow; the lower lobe is hazy. In the right side of the chest are dense shadows of indefinite outline extending out from the hilar and mediastinal regions; the bronchial markings are accentuated.

expansion; the right was resonant, except for substernal dulness and coarse râles; the left was flat with distant tubular breath sounds and râles.

Clinical Course.—There was a fever from 37.6 to 39.4 C. (99.6 to 102.8 F). There was progressive weakness, with more pronounced pulmonary signs; bronchial breath sounds were heard in the parasternal and interscapular regions. Dulness was present on the left, with flatness, bronchial breath sounds, and distant tubular breath sounds anteriorly; râles were present.

Laboratory Data.—No tuberculin reading was noted on the chart. The white blood cells numbered 8,400, with 60 per cent polymorphonuclears.

Roentgen Observations.—A roentgenogram was taken on April 26, 1926, two days before death (fig. 27). The left lung showed a dense homogeneous shadow

occupying the upper lobe except at the apex; the lower lobe showed mottled cloudiness. The right lung showed general mottled cloudiness and a dense shadow in the entire inner zone, extending from the hilar region outward to the middle zone, with an ill defined outline; there was bronchial marking throughout this shadow.

Postmortem Examination (Complete) (fig. 28).—There was generalized miliary tuberculosis. The lungs showed bilateral acute focal tuberculous pneumonia, with a large zone of consolidation in the lower lobe of the left lung. The bronchi showed tuberculous ulcerative bronchitis. The lymph nodes showed tuberculous bronchial lymphadenitis with erosion of and rupture into the bronchus of the left upper lobe. The nodes averaged 2 cm. in diameter. There were miliary tubercles in the viscera (liver, spleen and kidneys).

Fig. 28 (case 14).—The lungs and peribronchial lymph nodes. Bilateral focal tuberculous pneumonia is evident. Large caseous lymph nodes are seen.

Bacteriology.—B. tuberculosis was recovered from the lungs and lymph nodes (histologically).

Comment.—This infant was included in this group because, although there was definite and widespread parenchymal involvement, clinically and roentgenographically the involvement of the tracheobronchial lymph nodes seemed to be more important in precipitating death.

It is unfortunate that a roentgenogram was not taken just prior to death. In the one taken two days before (fig. 27) the dense shadow in the upper lobe of the left lung was thought to be caused by consolidation, and the physical signs seemed to confirm that. However, it was probably due to atelectasis brought about by the plugging of the

bronchus with the caseous contents of the tuberculous lymph node which was found at necropsy to have eroded and emptied into the bronchus (fig. 28). In the lower lobe of the left lung there was no roentgenographic evidence for the "large zone of consolidation" found at necropsy. In the right inner zone were large, irregular shadows which were cast presumably by the zones of pneumonia and by the peribronchial lymph nodes, although the latter were not clearly demarcated. Within the lower part of the shadow were to be seen the outlines of the dilated bronchi. There was nothing absolutely diagnostic of tuberculosis in these roentgenographic shadows, but with the clinical history and physical examination the presumptive diagnosis of tuberculosis was made and was confirmed at necropsy.

GENERAL COMMENT

The value of correlation of roentgenograms with the clinical and pathologic findings in fatal cases of tuberculosis in children should be emphasized. Experience in such studies affords the basis on which a correct anatomic and etiologic diagnosis from roentgenograms alone may be possible in many cases. This method of study is of greatest value when there are repeated roentgenograms taken under standard technical conditions over a period extending up to the time of death.[7] Certain aspects of roentgenographic technic which we believe are essential are described.[4]

In roentgenograms of children it is often difficult to diagnose pulmonary shadows as indicative of a tuberculous lesion even with the aid of the history, physical examination and laboratory data. Merritt [8] so concluded in her study of seventy-five infants under 1 year of age. Large homogeneous lobar shadows, mottled shadows (disseminated or localized) or so-called "infiltration" may or may not be caused by tuberculosis;[7] the interpretation of these shadows is often unduly influenced by a knowledge of the age of the patient and his reaction to tuberculin.

The presence of calcium deposits in the parenchyma, lymph nodes or pleura is indicative of a tuberculous process in a vast majority of instances. In this connection roentgenograms taken with oblique exposure are important for examination of areas not observable in the usual anteroposterior exposure.

Roentgenographic evidence of cavity formation is of equal importance with the presence of calcium in establishing a diagnosis of tuber-

7. Stewart, C. A.: Pulmonary Diseases: Five Thousand Eight Hundred and Sixteen Cases in Children, with Special Reference to the Childhood Type of Pulmonary Tuberculosis, Am. J. Dis. Child. **43**:803 (April) 1932.

8. Merritt, K.: Tuberculosis in Infants Under One Year of Age, Am. J. Dis. Child. **38**:526 (Sept.) 1929.

culosis. Recent writers have emphasized the tremendous advantage of the roentgenogram over physical examination in the detection of cavities. However, the caseous débris in a cavity often obscures the clinical as well as the roentgenographic signs of it even when it is very large. On the other hand, at times the roentgenograms may suggest cavities where there are none. It must be remembered that cavities in the lungs of children may occur in any lobe. These facts emphasize the necessity of repeated roentgenograms.

There is sometimes present in infants with tuberculosis an ulcerative bronchitis surrounded by consolidated lung;[9] these lesions are often in association with one or more cavities. The clinical symptoms of bronchiectasis may not be prominent, but in the roentgenogram the outlines of bronchi, often apparently dilated, within the shadow caused by the consolidation may be clearly seen. Even without the presence of cavities, this roentgenographic picture is strongly suggestive of a tuberculous lesion. It must be emphasized, however, that this picture is not produced exclusively by tuberculosis, for it is found occasionally in nontuberculous subacute or chronic, organized bronchopneumonias. As a general rule, however, the shadows produced by the nontuberculous bronchopneumonia with bronchiectasis do not have the smooth, homogeneous appearance (except for the bronchial markings) of the tuberculous consolidation. This is as one would expect since the tuberculous process is a diffuse parenchymatous lesion, whereas the nontuberculous pneumonia under discussion is a focal, peribronchial lesion. In roentgenograms of nontuberculous lobar consolidation the tracery of bronchi within the shadow cast by the solidified lung is sometimes seen but, in our experience, not frequently.

Occasionally the roentgenogram gives little indication of an extensive destruction of pulmonary tissue. Indeed, it may be pointed out here that a roentgenogram is sometimes essentially negative although the thorax of which the film is a projection is the seat of extensive and proved pathologic processes.

The generalized so-called miliary shadows or snow-flake infiltration frequently regarded as pathognomonic of generalized tuberculosis is sometimes closely simulated by certain forms of nontuberculous pneumonia. If these roentgenograms reveal no deposits of calcium and the snow-flakes are not sharply circumscribed, the only important differential point we have found has to do with the peripheral fields of the lungs; if these show disseminated areas of consolidation, the lesions are more likely to be of tuberculous etiology than if the peripheries are clear.

Although in pulmonary tuberculosis there is always an associated involvement of the tracheobronchial group of lymph nodes, the actual

9. Simon, G., and Blumenberg, W.: Pathogenesis of Bronchiectasis: Bronchiectasis and Tuberculosis, Beitr. z. Klin. d. Tuberk. **80**:234 (June 24) 1932.

diagnosis of tuberculous lymphadenitis from roentgenograms cannot, in our opinion, be made with such facility and frequency as the reports in the literature would indicate. From a technical standpoint, close target-film distance, rotation of the chest and the expiratory phase of respiration may bring about changes in the contour and size of the mediastinal shadow incorrectly suggestive of large lymph nodes.[4]

Calcium shadows in the mediastinal and hilar regions usually indicate the presence of tuberculous lymph nodes; frequently there is seen no accompanying shadow indicative of the lymph node itself, unless it is so located as to protrude beyond the normal cardiac, vertebral or mediastinal shadows. When, under proper technical conditions, a bulging hilar or mediastinal shadow of homogeneous density and well demarcated outline consistently appears in the roentgenograms taken from time to time of a child with a positive reaction to tuberculin, a diagnosis of tuberculous tracheobronchial nodes is warranted if there is no other explanation of the shadow; but only the presence of calcium in these shadows makes a purely roentgenographic diagnosis of tuberculous lymphadenitis highly probable.[7]

Clinically, tuberculous tracheobronchial lymph nodes may produce signs of bronchial obstruction either by compression of the bronchus from without or by the blocking of the lumen with material from a caseous lymph node which has eroded the bronchial wall and emptied its contents into the lumen. Roentgenographically, such phenomena give the usual evidence of a foreign body. Judging from our experience, these are not common occurrences.

The discussion presented is in no sense to be considered conclusive; an attempt has been made to bring out those points which were suggested by a study of our own material.

SUMMARY

The roentgenograms of fourteen tuberculous children were studied and correlated with clinical histories, laboratory data and postmortem records. There were seven boys and seven girls in the group, and all but two were under 2 years of age. Extensive pulmonary tuberculosis was present in eleven patients, six of whom had cavity formation; in two children there were disseminated tubercles; in one there was a chronic nontuberculous bronchopneumonia. In four children, tuberculous tracheobronchial lymphadenitis was the prominent lesion.

In each case individual comments on the interpretation of the roentgenograms have been made. Suggestions regarding roentgenologic technic for the type of patient under consideration are given.[4] The general conclusions reached as to the interpretation of the roentgenograms of the chests of tuberculous children are given in the general comment.

TUBERCULOSIS

II. PULMONARY TUBERCULOSIS IN INFANTS UNDER TWO YEARS OF AGE; A REPORT OF SEVEN CASES AND DISCUSSION OF THE COURSE OF THE DISEASE

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Seven infants in whom pulmonary tuberculosis developed before they were 2 years of age have been selected for report from a large group of tuberculous infants seen in the clinic for tuberculosis of the New Haven Hospital. They were selected because they had been followed up over a period of at least four years, during which time repeated clinical and roentgenologic examinations were made. A detailed analysis of these cases has been made to show the course of the disease, with the hope of throwing further light on the ultimate fate of infants infected at this early age. Few instances of recovery from pulmonary tuberculosis acquired in early infancy have been reported in which observation has been extended over a sufficiently long period to furnish reliable data on prognosis for those who survive the first or second year of life.

CLINICAL DATA

The case histories of the seven infants are given in detail at the end of the paper; the history and clinical findings when the infants were first seen are summarized in table 1. Four of the infants were under 1 year of age, and three were between 1 and 2 years when first seen; the youngest was 6 months, the oldest, 22 months of age.

All of the infants had a definite history of direct exposure to tuberculosis; in three cases the mother was the source of infection, and in one case each the father, a sister, a nursemaid and a cousin living with the family were the sources. Four of the persons to whom the infants were exposed were known to have positive sputums; the other three died of tuberculosis subsequent to the exposure of the infants.

From the Department of Pediatrics, Yale University School of Medicine, and the Pediatric Service of the New Haven Hospital and Dispensary.

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Just as knowledge of a possible source of infection may be helpful in making an early diagnosis of tuberculosis in infants, so knowledge of the extent and duration of exposure may be useful in prognosis. The exact duration or extent of exposure could not be definitely determined except in one case (case 6), in which it was certain that the exposure

TABLE 1.—*Summary of History and Findings on Admission to Clinic of Infants Under 2 Years with Pulmonary Tuberculosis*

Case	Age, Mos.	Exposure		Past History	Complaint; Present Illness	Physical Examination	Weight, pounds	Height, Inches
		Source	Duration					
1	9	Mother	Indefinite, probably 10 months	Diarrhea; otitis media; bronchitis	Swelling of right elbow	Pale; loose cough; signs of consolidation in right upper part of chest; osteomyelitis of right elbow; enlarged spleen	—	—
2	18	Sister	About six weeks	Cold and cough for one month	Contact; not doing well	Signs of consolidation in left upper part of chest; spleen palpable	22	32
3	7	Father	About seven months	Cough for one month	Contact; cough for one month	Poor muscular development; signs of consolidation in left upper part of chest; enlarged spleen	13	—
4	22	Nurse-maid	About two months	Negative	Contact; irritability; poor appetite; cough	Chest negative	—	—
5	6	Mother	About six months	Bronchitis for one month	Contact	Pale; poor muscular development; otitis media; enlarged spleen	13	—
6	9	Cousin	Two weeks	Not known	Repeated colds with cough and fever; loss of weight	Malnutrition; signs of consolidation in right upper part of chest and fluid at base of left lung; enlarged spleen	12¾	—
7	22	Mother	Indefinite, probably several months	Tuberculin test positive; cough for three months	Ill for ten days; less active; vomiting	Signs of fluid at base of right lung	25½	31¾

was not more than two weeks. The duration of exposure given in table 1 is, therefore, only approximate.

The past histories of five of the infants are of interest because all contained leads which, if followed up sooner, would in all probability have permitted the diagnosis of tuberculosis to have been made earlier. Three infants had a cough for from one to three months before admission, and attacks of bronchitis were reported in two. One of the latter had been ill with a gastro-intestinal disturbance and was under the observation of a physician for six months, but since it was not appreciated that the mother had tuberculosis, tuberculosis in the infant had not been suspected.

Four of the infants were brought to the clinic primarily because of known exposure to tuberculosis, but, on questioning, it was found that all of them had symptoms such as chronic or repeated respiratory infections, cough, irritability, loss of appetite and loss of weight which led the physician to suspect tuberculosis.

In each case the initial physical examination revealed certain evidences of illness which in themselves were not pathognomonic of tuberculosis. In general, the infants were not markedly underweight for their height, only one infant being described as "malnourished." Pallor of the skin was an almost constant finding; the mucous membranes, however, were not correspondingly pale, nor did examination of the blood in any case show a marked degree of anemia. In four cases the musculature was described as "flabby," and there was a curious apathy or gentleness which disappeared as improvement began. Four infants showed slight and two moderate enlargement of the cervical lymph nodes, which was associated with enlargement of the tonsils in five cases. The infant with tuberculous osteomyelitis of the ulna (case 2) had enlarged epitrochlear nodes. Enlargement of the spleen was not a constant finding, occurring in only four of the seven infants. It was palpable in one child, and not felt in two.

Clinical examination of the chest made at the time of admission showed abnormal findings in five of the seven infants. In each of these, percussion changes were easily made out, and were found in sharply defined areas that were more or less extensive. The degree of impairment of the percussion note usually corresponded fairly well with the denseness of the areas of parenchymal involvement shown by roentgenograms.

The breath sounds over these dull and impaired areas, even in the absence of fluid, were strikingly diminished in intensity. In one case only was tubular breathing heard, such as one expects to find over areas of consolidated lung, and even in this case it was distant.

On examination of the chest, râles were heard in three cases, but were absent on repeated examination in four. In one infant (case 1) coarse rhonchi were heard on the initial examination only; in another patient (case 6) râles were heard repeatedly on examinations of the chest made during the first few days, but not on subsequent examinations; in a third infant (case 7) pleural râles were heard at the time of admission, but disappeared with the accumulation of fluid.

ROENTGENOGRAMS

Roentgenograms were taken in every case at the time of admission. In five cases the roentgenographic findings corresponded with the physical findings; in two cases in which the roentgenograms showed evidence of lesions corresponding physical signs were not found.

The roentgenograms taken in these cases at the time of admission to the clinic have been grouped according to the character of the shadows cast by the pathologic process in the lungs.

In the first group (cases 1 and 2) the roentgenograms showed the presence of dense homogeneous shadows involving part or all of one or more lobes with sharply defined lower borders. In case 1 (fig. 1 *A*) the whole upper lobe of the right lung appeared to be consolidated; the lower border was sharply defined and curved downward as if possibly the volume of this lobe was increased. In case 2 the shadow in the upper lobe of the left lung was dense, but less so than that in case 1, while the extreme apex was relatively clear (fig. 2). As in case 1, the lower border of the shadow was well defined and convex. The opposite lung in each case was relatively clear. The roentgenographic findings in these two cases correspond to those described by Eliasberg and Neuland [1] as typical of epituberculosis.

In the second group (cases 3, 4 and 5), the roentgenograms showed less sharply circumscribed parenchymal involvement. The roentgenogram in case 3 (fig. 3) differs from those in the first group in that the shadow at the upper lobe of the left lung was less sharply defined, and there were in addition dense areas scattered throughout both lungs which were suggestive of disseminated tuberculosis. At no time, however, were clinical signs found on the right side, or indeed on the left side, outside of the dense area in the upper lobe. The roentgenogram in case 4 showed a dense shadow that appeared to be spreading from the hilus into the upper lobe of the right lung, and also mottling in the inner zone of both lungs (fig. 4). In case 5 the roentgenograms showed a wide mediastinal shadow and mottling in both hili, which were more marked on the left. A diagnosis of pulmonary tuberculosis was not made at this time. Though the clinical examination of the lungs gave negative results, the tuberculin test was positive, and the sputum contained acid-fast bacilli. In a roentgenogram taken two months later, however, definite evidences of more extensive parenchymal involvement were seen extending out from the left hilus (fig. 5). Repeated films thereafter showed no further extension of this process, and at no time did physical examination reveal the changes in the lungs.

In the third group (cases 6 and 7) the roentgenograms showed evidences of pleurisy. In the first film taken in case 6, there was evidence of widespread bilateral involvement of the parenchyma as well as a dense shadow with a poorly defined upper border, suggesting the presence of fluid at the base of the left lung (fig. 6 *A*). The clinical signs present at the base of the left lung seemed to corroborate this,

1. Eliasberg, H., and Neuland, W.: Die epituberkulöse Infiltration der Lunge bei tuberkulösen Säuglingen und Kindern, Jahrb. f. Kinderh. **93**:88, 1920.

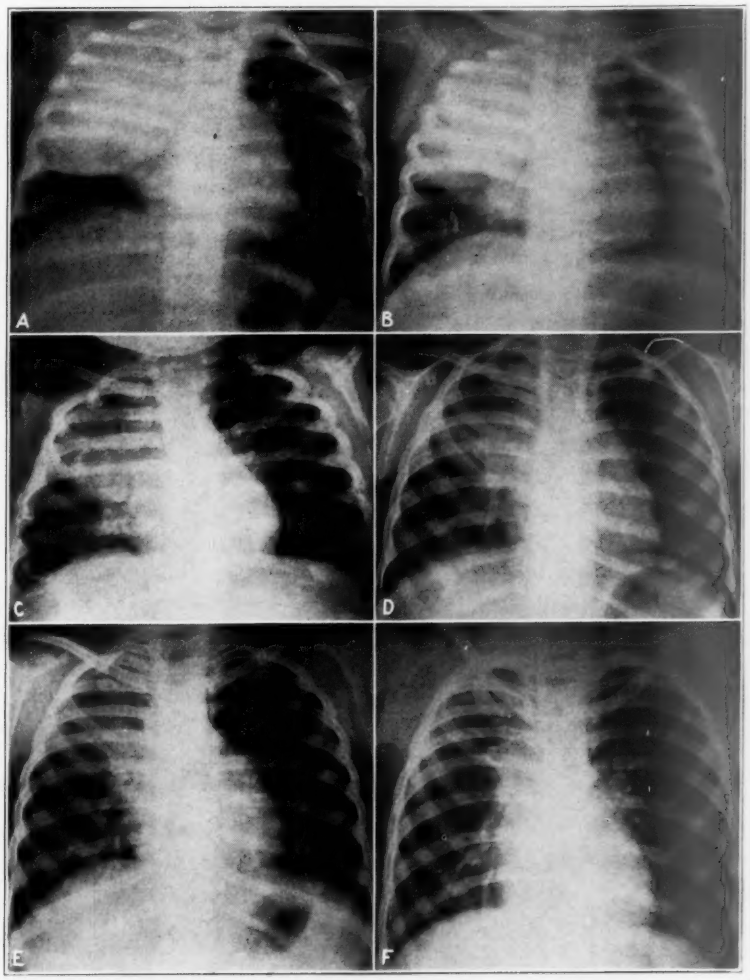

Fig. 1.—*A* shows a very dense homogeneous shadow with a sharp convex lower border occupying the upper two thirds of the right lung. *B* was taken two months later and shows the dense shadow almost unchanged with a mottled area of extension downward. In *C* the shadow on the right has become thinner, and dense mottled areas of calcification have appeared in the parenchyma. In *D* the shadow of consolidation has disappeared. The areas of calcification have become smaller but more dense. The interlobar fissure is faintly outlined and is concave. In *E* a thin homogeneous shadow has appeared on the right, involving the upper third of the lung. All evidence of calcification has disappeared. In *F* the large sharply defined area of decreased density in the upper lobe of the right lung suggests cavitation.

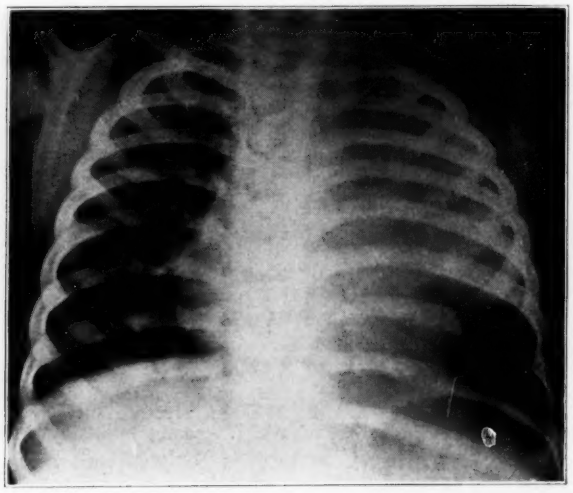

Fig. 2.—A dense shadow involves the upper two thirds of the left lung.

Fig. 3.—An area of increased density involves the lower part of the upper lobe of the left lung; the apex is relatively clear; there is marked mottling throughout the right lung.

but a thoracentesis was not performed. In a film taken six months later, however, a line was seen on the left side marking a reflection of the pleura, obviously the result of a pleural effusion. In case 7 the

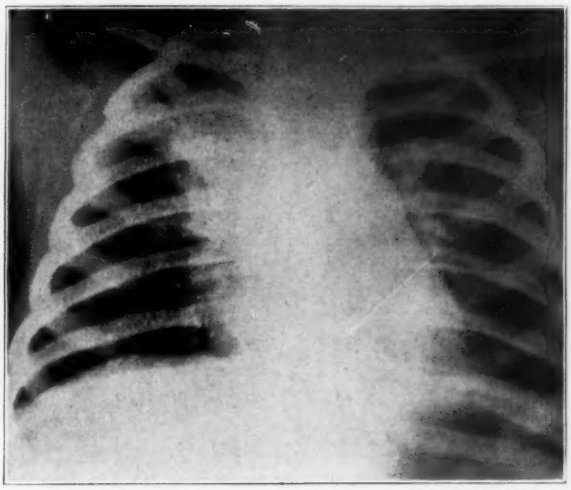

Fig. 4.—A shadow of ground-glass density appears to be spreading from the hilus toward the apex of the right lung.

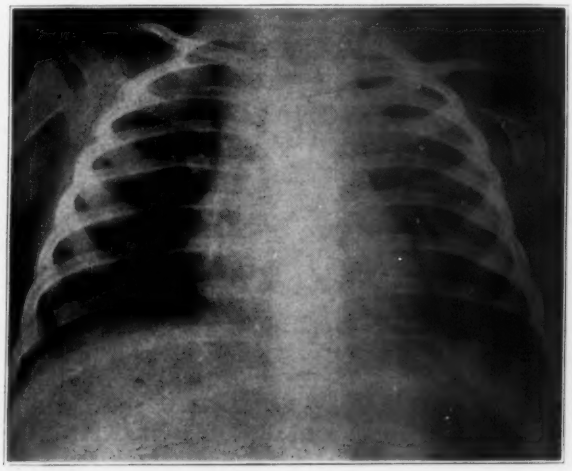

Fig. 5.—An area of increased density in the left hilus is extending toward the apex.

roentgenogram taken on admission showed a more or less uniform density covering about two thirds of the right side of the chest, the density being greatest at the extreme base with a fluid level at the upper and lateral margins (fig. 7 *A*).

In the seven cases roentgenograms were taken at intervals throughout the period of observation. By study of these films the course of pulmonary tuberculosis in these infants has been followed for periods of four or five years. Case 1 illustrates most strikingly the changes that take place during the course of the disease, when parenchymal involvement is such as to cast dense circumscribed shadows on the roentgenogram. The changes seen in the films are described in detail

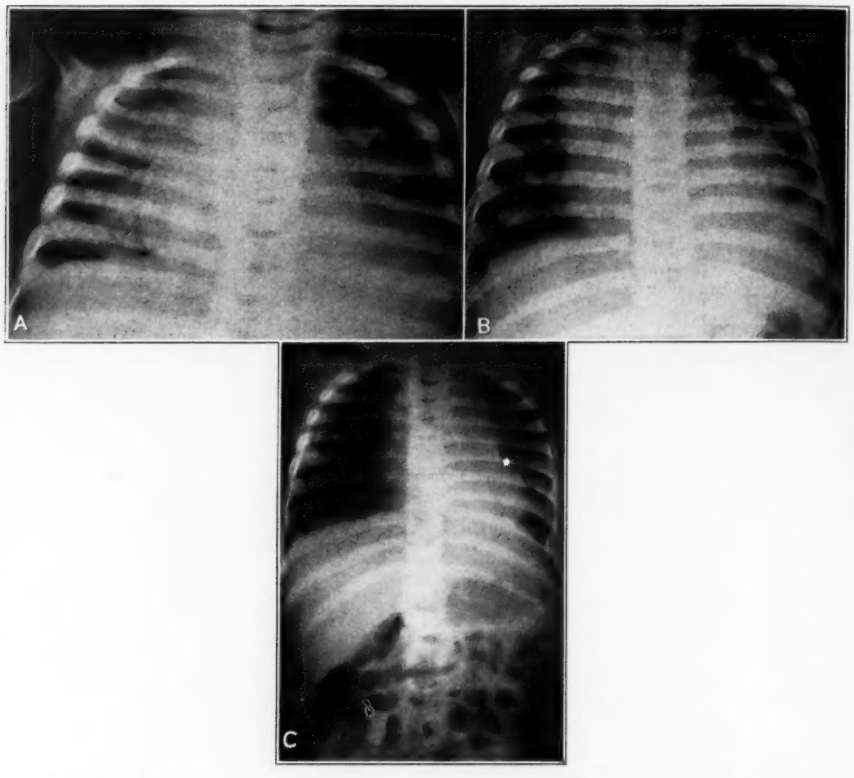

Fig. 6.—*A* shows heavy dense mottling throughout the right lung and in the upper lobe of the left lung. There is a dense shadow involving the base of the left lung, with a poorly defined upper border suggesting the presence of fluid. *B* was taken six months after *A*. There is a line of pleural reflection on the left. The mediastinal shadow is increased in width. *C* shows calcification in the pleura and spleen.

since they bring out many points of interest. A series of six roentgenograms covering a period of more than four years is shown in figure 1. The roentgenogram shown in figure 1 *A* was taken on admission, when the patient was 9 months old, and shows a dense shadow extending over about two thirds of the right lung, with its lower border curved downward. Figure 1 *B*, from a roentgenogram taken about two months

later, shows the same shadow persisting almost unchanged and, in addition, a mottled area extending from the right hilus downward. Roentgenograms taken six months after admission (not reproduced) showed that the dense shadow had become less extensive, as though the consolidated area had shrunk. During the course of the next seven months this shadow became less dense, and within it there appeared a dense mottled area interpreted as that of calcification, shown in figure 1 *C*. Other smaller areas of calcification were seen in the hilus on the right side. At the end of eighteen months of observation, when the infant was 27 months old, a roentgenogram showed that the shadow in the upper lobe of the right lung had disappeared. A discrete circular calcified node below the second rib near the right sternal border as well as small well defined areas of calcification at the lower border of the upper lobe in the midzone were seen for the first time (fig. 1 *D*). The interlobar fissure was clearly visible and tended to curve upward, as

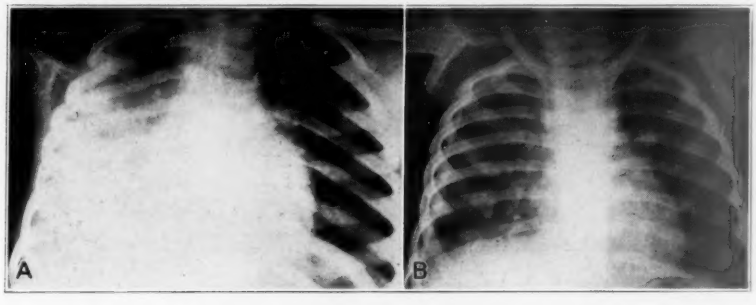

Fig. 7.—In *A* the shadow extends over the lower two thirds of the left lung, with the greatest density at the base. In *B*, the line of pleural reflection is still visible, one year after the acute illness.

though there had been shrinkage of the lung. A roentgenogram taken about one and a half years later, at the time of a reappearance of the symptoms of illness, showed that the areas of calcification seen in figure 1 *D* had practically disappeared, but a homogeneous shadow had reappeared at the upper lobe of the right lung. The interlobar fissure on the right was still clearly defined (fig. 1 *E*). A roentgenogram taken at the age of 5 years showed bilateral hilar and peribronchial infiltration as well as an area of decreased density with a sharp outline in the upper lobe of the right lung, suggesting a cavity (fig. 1 *F*).

Roentgenograms were also taken at varying periods after admission in the other six cases and will be referred to further in the discussion of the course of the disease.

Thinning or rarefaction and contraction of the dense shadows seen in the upper parts of the lungs are, probably, the first evidences of improvement that can be shown by repeated roentgenographic exami-

nation in cases of massive consolidation of the lungs. Next, as these shadows decrease in size and density, other denser shadows, probably those of areas of calcification, appear and show in the roentgenogram either as mottled, honeycombed or mulberry-like areas or as conglomerate masses. Shadows of areas of calcification were seen in roentgenograms sooner or later in six of the seven cases followed, and were still evident at the last examination in four. In the two cases (cases 1 and 3) in which evidences of calcification in the parenchyma of the lungs disappeared, signs of activity of the disease reappeared later. In one case (case 1), as already pointed out, there was an extension or flare-up of the pulmonary lesion followed by the development of signs of cavitation (fig. 1 *F*). In the other case (case 3) dissemination of the disease resulted in death from tuberculous meningitis. Evidence of calcification was most marked in case 6. Roentgenograms taken fifteen months after the patient's admission to the hospital showed extensive calcification of the pleura on the left side; one month later small areas of increased density were also visible in the region of the spleen (fig. 6 *C*), and two months later still the pleura on the left was studded with areas of density that were thought to be deposits of calcium.

In one of the two cases (case 7) in which pleurisy with effusion occurred, the line of pleural reflection was visible for twelve months. In case 6 the appearance of mottled areas of increased density was interpreted as calcification in the pleura (fig. 6 *C*). In case 7 no evidence of calcification of the pleura has been demonstrable by roentgenograms, but a circular area of increased density about the size of a five cent piece, interpreted as a calcified lymph node in the parenchyma, was seen in the midzone at the base of the right lung in the last film taken at the age of 5 years. These two cases, which are grouped together because of the occurrence of a pleural effusion, can scarcely be discussed together because the other roentgenographic findings were so different. In case 6 evidences of extensive parenchymal involvement as well as involvement of the tracheobronchial lymph nodes were present, while in case 7 the evidences of fluid were outstanding but there was very little evidence of either parenchymal involvement or involvement of the lymph nodes. As the fluid cleared evidences of parenchymal involvement appeared, however, and the line of pleural reflexion was clearly seen (fig. 7 *B*). In a later film the lower part of the right bronchus appeared to be dilated, and along its course the pulmonary field, as well as the region of the left hilus, showed a ground-glass appearance. The significance of these changes is not yet apparent.

In the cases in which the only pathologic finding was a sharply defined dense area in the upper part of one lung (cases 1 and 2) there was nothing characteristic in the roentgenogram taken on admission that

would permit one to make a diagnosis of tuberculosis. A differential diagnosis between tuberculosis and lobar pneumonia on the basis of the roentgenogram alone would be difficult. When the infant is first seen the clinical history may or may not help in the diagnosis. The presence of additional signs in the roentgenogram, such as enlargement of the hilus, a shadow most marked at and appearing to spread from the hilus toward the apex or fine mottled areas of increased density in the lung outside the sharply defined dense area, should always suggest the possibility of tuberculosis. The most valuable roentgenologic evidence of tuberculosis is the appearance of calcified areas in the parenchyma

TABLE 2.—*Laboratory Data*

Case	Date of Admission	Tuberculin Test	Examinations for Acid-Fast Bacilli			Examination of Blood on Admission	
			Sputum	Gastric Content	Other Examinations	Red Cells	Hemoglobin
1	12/17/24	+0.02 mg.	0 (2/28/31)	0 (2/28/31)	Pleural fluid 0 (12/19/24) Pus from elbow 0 (4/19/25)	4,404,000	70
2	7/14/27	+0.1 mg.	.....	0 (8/6/27)	.....	4,000,000	50
3	10/21/26	+0.02 mg.	0 (1/30/28)	+ (11/2/26) 0 (1/22/27)	Stool 0 (10/29/26) Urine + (1/—/28) Spinal fluid + (5/18/31)	5,500,000	77
4	7/28/27	+0.1 mg.	.....	.....	.....	.....	..
5	9/ 4/26	+0.02 mg.	.....	+ (11/ 2/26) 0 0	.....	4,160,000	75
6	6/11/27	+0.02 mg.	0 (6/12/27) 0 (7/11/27) + (9/17/28)	+ (6/14/27) 0 (1/ 6/28) 0 (11/19/30)	.....	5,200,000	95
7	3/31/27	+0.01 mg.	.....	0 (12/7/27)	Pleural fluid + (11/11/27)	4,376,000	80

or at the hilus. A series of roentgenograms, together with a knowledge of the clinical course and other laboratory findings, is usually necessary to make the diagnosis of tuberculosis.

OTHER LABORATORY EXAMINATIONS

The laboratory data are shown in table 2. Intradermal tuberculin tests (Mantoux) were made on all of the infants, and the first test was positive in each case. Dilutions of old tuberculin,[2] from 0.01 to 0.1 mg., were used; the injections were made into the flexor surface of the forearm, and the results were read at the end of forty-eight hours.

The sputum was examined in three cases, and tubercle bacilli were found in one (case 6). The contents of the stomach during fasting,

2. Old tuberculin was obtained through the courtesy of the National Tuberculosis Association from the research laboratory.

which were examined in six cases according to the method described by Armand-Delille,[3] yielded "positive" results in three (cases 3, 5 and 6); that is, acid-fast organisms with the morphology of the tubercle bacillus were demonstrated in smears. Many unsuccessful attempts were made to grow the organisms from the stomach washings in these three cases. Repeated cultures of the stools were also made, but acid-fast bacilli could not be grown. According to the criteria of Armand-Delille, the infants had "positive" sputums, but the value of the examination, in my opinion, is weakened by the fact that the organisms could not be grown. The urine in one case (case 3) when inoculated into a guinea-pig gave a positive result. The pleural fluid in one case (case 7) when inoculated into a guinea-pig was proved to be tuberculous. In one case (case 1) a drop of fluid was obtained by a diagnostic tap, but organisms were not found in smears.

COURSE

The course of the disease in all of these infants has been strikingly similar in many respects. Increase in weight has been slow and the curve was characterized by periods of gain alternating with periods in which the weight did not change or loss of weight occurred. During the whole period of observation there was a net gain in each case, but the weight at the time of this report is below the average with one exception in which the child (case 5) is overweight.

Fever was not always present even in the early stages of the disease. The temperature in four of the cases during the period in the hospital was usually normal or subnormal, with occasional sharp rises caused apparently by acute infections of the upper respiratory tract. In one case (case 2) daily fever was present for the first three weeks that the patient was in the hospital, and in one case (case 7) for the first week, after which the temperature remained normal except for occasional transitory rises. In one case (case 5) fever was present almost daily throughout the course of the disease (four years).

The infants were kept in bed over prolonged periods. They all received intensive treatment with ultraviolet rays and direct sunlight; all were given cod liver oil. Repeated transfusions of blood were given to two infants (cases 1 and 4) early in the course of the disease, with the hope of improving the general condition and perhaps of increasing the resistance to the disease.

In four cases evidences of tuberculosis other than pulmonary developed. In three infants lesions of the skin developed which were diag-

3. Armand-Delille, P. F.: Pulmonary Tuberculosis in Infants: Bacteriologic Diagnosis by Examination of the Stomach Contents, Am. J. Dis. Child. **34**:547 (Oct.) 1927.

nosed clinically in two cases as papulonecrotic tuberculids, and in the third as scrofuloderma. One infant (case 6) in whom clinical evidence of peritonitis developed which lasted several weeks made a spontaneous recovery. One infant had osteomyelitis of the ulna (case 1), and one osteomyelitis of the spine (case 9). In one infant meningitis developed (case 3).

The present condition of the seven infants and the results of the most recent clinical and roentgenographic examinations are shown in table 3.

Four infants are considered well and are at home (cases 2, 4, 5 and 7). The last examination of the lungs gave evidence of parasternal dulness in all four of these cases. The last roentgenographic examination of the chests showed calcification of the lymph nodes in all four cases, "Dunham's fan" in two, infiltration of the hilus in three and thickening of the interlobar fissure on the right in one.

Two infants are in sanatoriums for tuberculosis (cases 1 and 6). Clinical as well as roentgenographic evidences of tuberculosis are still present in these cases.

One infant (case 3) died at the age of 4 years and 7 months. He had been under treatment in a sanatorium for tuberculosis when signs of meningitis developed. Examination of the spinal fluid showed tubercle bacilli. The roentgenogram taken just before death showed prominence of the left hilus, a thickened pleura and peribronchial infiltration on the left, with absence of evidences of calcification in the lymph nodes and parenchyma.

REVIEW OF THE LITERATURE

Although numerous articles dealing with the subject of tuberculosis in infancy have appeared in the literature, reports of cases of pulmonary tuberculosis in infants under 2 years of age are comparatively rare. The largest series, one of one hundred and thirty cases, was reported by Hempelmann.[4] The diagnoses were based on "the presence of symptoms, pathological physical findings, positive tuberculin reaction, and positive roentgenographic findings, the presence of all four being a necessary requisite for admission to the series. The only exceptions to this were those cases in which the infants died and the diagnosis was confirmed at autopsy." Of the one hundred and thirty children, sixty-four died, and only thirty are known to have lived for a period of more than one year after the diagnosis was made, although some of these were observed for periods of from four to five years.

4. Hempelmann, T. C.: The Progress of Pulmonary Tuberculosis in Infancy, Am. Rev. Tuberc. **1**:99, 1917.

TABLE 3.—*Present Condition of Infants Based on Clinical and Roentgenographic Findings*

Case	First Observation		Last Observation						Comment
	Date	Age, Months	Clinical Findings	Date	Roentgenographic Findings	Date	Weight, Pounds	Height, Inches	
1	12/16/24	9½	Impaired percussion note in right infraclavicular region; amphoric breath sounds	1/ 8/31	Bilateral hilar and peribronchial infiltration; sharply defined interlobar pleural line displaced upward; area of decreased density in upper lobe of right lung suggests cavitation	1/ 8/31	45¼	..	In sanatorium for tuberculosis
2	7/14/27	20	Slight parasternal dulness	9/10/32	"Dunham's fan" and tentlike shadow on left; shadow of calcified lymph node in right hilus	2/21/31	55	47½	Home; going to school
3	10/21/26	7	Tuberculous meningitis	5/ 8/31	Diffuse infiltration of both pulmonary fields; marked prominence of hilar shadow on left; no evidence of calcification	5/20/31	30½	..	Died of tuberculous meningitis
4	7/ 8/27	22	Tubular breath sounds and increased breath sounds to right of sternum	12/16/31	Triangular shadow projecting from right hilus continuing into interlobar pleural line, which has upward convexity; deposition of calcium in upper lobe of right lung; peribronchial infiltration on right; hilar infiltration on left	12/16/31	..	..	Home; going to school
5	7/20/26	6½	Parasternal dulness	1/14/31	Right peribronchial infiltration; "Dunham's fan" on left; deposition of calcium in lymph nodes behind sternum seen in oblique view	1/14/31	39	41	Home; going to school
6	6/11/27	9	Osteomyelitis of spine; impaired percussion note; diminished breath sounds and fine moist râles on left side of back	11/ 7/30	Widespread deposition of calcium in both lungs; mediastinum broad; bilateral parenchymal infiltration	4/16/30	37½	..	In sanatorium for tuberlosis
7	3/31/27	22	Slight parasternal dulness	11/ 4/31	Ground-glass infiltration opposite left hilus and along dilated right lower bronchus; broad mediastinum; shadows of calcified lymph nodes in left hilus and at base of right lung	7/21/30	43½	44	Home; going to school

Eighty-two other cases of pulmonary tuberculosis in infants under 2 years of age have been reported by twenty-six authors, fifteen of whom reported one case only. Although in each case the tuberculin test was positive, the other criteria on which the diagnoses were made varied somewhat and were not as a rule as complete as in the cases reported by Hempelmann. The period of observation, when stated, varied between a few days and several years.

In all, only twenty-three case reports have been found in which the period of observation was four years or longer.[5] The ages of the infants at the time the diagnosis was made varied between 2 months and 2 years. The intradermal tuberculin test was positive in six cases and the Pirquet test in eleven cases; no test was reported in six cases. Signs of involvement of the lungs were described in eighteen of the twenty-three cases. The diagnosis was made by roentgenographic examinations in nineteen of the twenty-three cases; in four no records of roentgenographic examinations were found. The sputum was examined in three cases, but was found to be positive in only one. Puncture of the lungs, which was made in two cases, gave negative results; a culture of the pleural fluid, made in one case, was negative; the stools were examined in one case and the results were negative.

The period of observation in the twenty-three cases varied between four and eleven years. Clinical examination of the lungs made at the end of the period was recorded in only six. The lungs were reported as negative, normal or clear in five of the six cases; in one case "lagging" of the left side of the diaphragm was found. In two of the cases in which the lungs were normal, D'Espine's sign was recorded as "positive."

Roentgenographic findings were recorded in seventeen of the twenty-three cases at the time of the last examination. In no case was any evidence of parenchymal involvement found. Calcification of the lymph nodes in the hilar region was present in ten cases; in two, movement

5. Hempelmann.[4] Ribadeau-Dumas, L., and Béclerè, H.: Evolution de la lésion initiale de la tuberculose pulmonaire chez l'enfant du premier âge, Bull. et mém. Soc. méd. d. hôp. de Paris **43**:651 (July) 1919. Osswald, R.: Zur Prognose der Säuglingstuberkulose, Monatschr. f. Kinderh. **23**:168 (May) 1922. Langer, H.: Die Prognose der Säuglingstuberkulose, München. med. Wchnschr. **70**:76 (Jan. 19) 1923; Tuberkuloseerkrankungen in den ersten Lebensmonaten, Beitr. z. Klin. d. Tuberk. **64**:515, 1926. Kohn, J. L.: Tuberculous Infection of the Lung in Early Infancy, Am. Rev. Tuberc. **17**:565, 1928. Spence, J. C.: Benign Tuberculous Infiltration of the Lung (Epituberculosis), Arch. Dis. Childhood **7**:1 (Feb.) 1932. Weech, A. A., and Chu, F. T.: Pulmonary Tuberculosis of the Epituberculous Type, Nat. M. J. China **16**:1, 1930. Stewart, C. A.: Pulmonary Diseases: Five Thousand Eight Hundred and Sixteen Cases in Children, with Special Reference to the Childhood Type of Pulmonary Tuberculosis, Am. J. Dis. Child. **43**:803 (April) 1932.

of the diaphragm was impaired on one side; in one the hilus was enlarged; in two the roentgenograms were said to show nothing abnormal.

In six cases neither physical examination nor roentgen findings were recorded, but a general statement was made as to the child's condition, such as "in good condition" or "well."

PROGNOSIS

From a study of the literature as well as of the seven cases reported, it is obvious that the ultimate fate of infants under 2 years of age who have pulmonary tuberculosis is difficult to prognosticate. Early reports based almost entirely on hospital statistics undoubtedly exaggerated the mortality of the disease in this early age period. With earlier diagnoses made possible by the wider use of the tuberculin test and roentgenographic examination and with the more careful follow-up of infected infants, the generally bad prognosis commonly given in cases of tuberculosis among children under 2 years of age undoubtedly should be modified. Since the publication in 1920 of the work of Eliasberg and Neuland,[1] the tendency has been to give a favorable prognosis in certain cases differentiated by these authors on clinical and roentgenographic findings as cases of "epituberculosis."

Park[6] stated:

> It is most difficult to say what the prognosis is in the tuberculosis of infants and any figures given are guesses on my part. As our experience with tuberculosis in infants increases, the more aware we are that recovery very frequently takes place. But the danger to the infant of tuberculous infection is exceedingly great. Probably 50 per cent of those infected under 6 months of age die, and probably 30 per cent of those infected under the age of 1 year.

From a study of the seven cases reported it would appear that tuberculosis in infants is not invariably fatal, but may be a chronic disease. The fact, however, that a child is alive at the end of four years does not mean that the ultimate prognosis is good.

SUMMARY

Seven cases of pulmonary tuberculosis in infants are reported, the diagnosis having been made in each instance when the patient was under 2 years of age. All of the infants had positive tuberculin tests (Mantoux) and showed evidence of pleural or parenchymatous involvement in roentgenograms. Repeated roentgenographic examinations gave valuable information in regard to the progress of the disease.

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6. Park, E. A.: Primary Tuberculous Infection in the Infant, South. Med. & Surg. **91**:449 (July) 1929.

The period of observation in each case was between four and five years.

Four of the children are considered well at the present time; two are still under treatment for tuberculosis; one died of tuberculous meningitis at the age of 5 years.

Reports in the literature of infants in whom pulmonary tuberculosis developed before the age of 2 years and who have been followed up for four years or more are relatively few in number.

CONCLUSIONS

Pulmonary tuberculosis in infants under 2 years of age is not necessarily fatal, but even after a long period of observation a very guarded prognosis should be given.

A still larger number of infants will have to be carefully studied over a period of years before sufficiently reliable data will be available as a basis for prognosis.

REPORT OF CASES

CASE 1.—A. K., a white girl, born on Feb. 28, 1924, was admitted to the Dispensary on Dec. 17, 1924, at the age of 10 months, because of swelling of the right elbow following a fall. The mother, 45 years old, had been in a sanatorium for tuberculosis but at the time of admission of the patient to the hospital, she was at home. Tubercle bacilli had been found in her sputum in December, 1920. The infant was well until 3 months of age, when diarrhea developed which persisted for five months in spite of treatment. At 4 months she had suppurative otitis media. She had also had rickets and bronchitis.

On examination, the temperature was 38 C. (100.4 F.). The infant was pale and irritable, and had a loose cough; the fontanel was soft and slightly depressed; the percussion note was dull over the right upper part of the chest anteriorly and in the right axilla down to the third rib, with tubular breathing just below the right clavicle; the spleen was slightly enlarged. There was a diffuse swelling below the right elbow joint, with bilateral enlargement of the epitrochlear lymph nodes. The intradermal tuberculin test (0.02 mg.) was positive. A roentgenogram showed marked density throughout the upper two thirds of the right lung. The diagnosis was pulmonary tuberculosis and tuberculous osteomyelitis.

The temperature was elevated for about three weeks; then it became normal and remained so except for occasional rises to 38 C. (100.4 F.) or slightly above, apparently associated with infections of the upper respiratory tract. Abscesses developed beneath the chin and also over the left ulna. The infant had German measles and chickenpox while in the hospital without any apparent effect on her pulmonary condition. She gained weight slowly. She was discharged to her home on Oct. 6, 1927, but continued under observation in the outpatient clinic for tuberculosis. In June, 1928, she was readmitted to the New Haven Hospital for heliotherapy, and while there follicular tonsillitis developed. Two weeks later her adenoids and tonsils were removed. In September, 1928, she was sent to a sanatorium, from which she was discharged the following April. During the summer of 1929 she again spent three months in a sanatorium. In June, 1930, signs interpreted as those of cavitation developed in the right lung and were confirmed by

roentgenographic examination. Two examinations of the gastric contents gave negative results for tubercle bacilli. The temperature was normal except for occasional rises to 38 C. (100.4 F.) or a little above. The patient is still under treatment in a sanatorium.

CASE 2.—C. A., a colored boy, born on Nov. 15, 1925, was admitted to the New Haven Hospital on July 14, 1927, at the age of 20 months, because of fever, listlessness, irritability and a cough of about one month's duration. A sister who was known to have active pulmonary tuberculosis had returned home from a sanatorium six weeks previously. The infant had been examined in the dispensary one month previously because of known contact with his sister. The examination at that time showed only mild rickets. An intradermal tuberculin test (0.02 mg.) was negative, and a roentgenogram of the lungs showed nothing abnormal.

On examination the temperature was 38 C. (100.4 F.); the weight, 10,240 Gm., and the height, 80 cm. The infant was rachitic but well nourished and did not appear very ill. There was marked enlargement of the cervical lymph nodes; the tonsils were enlarged and red. The percussion note was impaired over the left upper part of the chest anteriorly down to the midscapular region; over these areas the breath sounds were distant, there was no tubular breathing, and no râles were heard. The tip of the spleen was just palpable. An intradermal tuberculin test (0.1 mg.) was positive; a roentgenogram showed a dense shadow in the left side of the chest. A diagnosis of tuberculous pneumonia was made.

While the patient was in the hospital, the temperature was usually normal, but rose nine times to 38 C. (100.4 F.) or slightly above. The appetite was usually good. Cod liver oil was given, and he received exposure to the sun. Tuberculids of the skin developed. The gastric contents were examined during fasting for tubercle bacilli, but none were found. The infant remained in the hospital for six weeks, during which time he gained 2½ pounds (1,133.9 Gm.) although the signs in the lungs as well as the appearance of the roentgenograms were practically unchanged. He was sent to a sanatorium on Sept. 10, 1927, where he remained until March 1, 1930. The roentgenogram was reported to show a "calcified focus in the upper portion of the left lung" and "attending calcification of the lymph nodes." Since discharge from the sanatorium he had been under observation in the dispensary clinic. In September, 1930, whooping cough developed; in May, 1931, he had bronchitis; in July, 1931, the adenoids and tonsils were removed; in December, 1931, he had an infection of the upper respiratory tract with mild cervical adenitis; in January, 1932, he had mumps. In March, 1932, he had a cough, the temperature was 98.6 F., the weight was 53½ pounds (24,267.6 Gm.), and the height was 45½ inches (115.5 cm.). Examination of the lungs at this time showed parasternal dulness with an expiratory wheeze and a few scattered râles at the bases of both lungs. The last roentgenogram, taken on Feb. 21, 1931, at the age of 5¼ years, showed a "prominence of the left hilus shadow with an area of increased density radiating out into the midzone of the lung, suggesting a bilateral tuberculous process."

CASE 3.—C. M., a white boy, born on March 29, 1926, was admitted to the New Haven Hospital on Oct. 21, 1926, at the age of 7 months, because of contact with the father, who was known to have active pulmonary tuberculosis and positive sputum, and because the infant had a cough.

On examination the temperature was 37 C. (98.6 F.); the weight, 6,000 Gm. The infant was fairly well nourished; the color was good but the muscular development was poor; the tonsils were moderately enlarged and injected; the percussion note was impaired over the upper left part of the chest, front and back;

the breath sounds were distant over this area, no râles were heard; the spleen was two fingerbreadths below the costal margin. The intradermal tuberculin test (0.02 mg.) was positive; a roentgenogram of the lungs showed density from the apex of the left lung to the sixth rib; on the right there was mottling throughout, like that seen in miliary tuberculosis.

Throughout the period in the hospital the temperature was usually normal, with occasional rises to 38 C. (100.4 F.) or slightly above, thought to be due to infections of the upper respiratory tract. Several transfusions of blood were given early in the course, when the infant was vomiting and seemed to be doing poorly. The appetite was capricious. A high caloric diet, cod liver oil, ultraviolet irradiation and exposure to sunlight were given. There was a gradual increase in weight, resulting in a total gain of 7 pounds (3,175.14 Gm.) in the sixteen months in the hospital. On Feb. 2, 1928, twenty-three months after admission to the hospital, the infant was sent to a sanatorium. In May, 1931, he became acutely ill with fever, vomiting and abdominal pain, and was readmitted to the New Haven Hospital, where a diagnosis of tuberculous meningitis and pulmonary tuberculosis was made. Tubercle bacilli were demonstrated in the spinal fluid; a roentgenogram of the lungs showed a prominent left hilus and thickened pleura on the left side. Death occurred four days after admission. Autopsy was not permitted.

Case 4.—M. M., a white girl, born on Sept. 15, 1925, was first seen on July 8, 1927, at the age of 22 months, because of a positive Pirquet test. In March, 1927, the infant was cared for by a nurse who had a cough. Two months later tubercle bacilli were found in the sputum of the nurse, whereupon she was discharged. Toward the middle of June, three months after exposure and about three weeks before admission, the infant became irritable and restless at night, and had a poor appetite, and recently a dry cough had developed.

On examination the infant was fairly well nourished but irritable and therefore difficult to examine. The tonsils were enlarged and slightly red; the cervical lymph nodes were palpable; no definite signs in the lungs were made out; the spleen was not palpable. A roentgenogram showed infiltration of the upper lobe of the right lung. A diagnosis of pulmonary tuberculosis was made.

The child was sent to a sanatorium, where she remained for five months in bed. She had daily fever but gained weight. On Dec. 15, 1927, she entered the New Haven Hospital with an acute respiratory infection characterized by high fever, rhinitis and cough of five days' duration. A diagnosis of bronchopneumonia and acute bilateral suppurative otitis media was made. The roentgenogram taken at this time showed an extension of the infiltration of the upper lobe of the right lung. The acute symptoms subsided rapidly, and after sixteen days in the hospital she was discharged to a sanatorium, where she remained in bed for several months and then returned to her home. In June, 1929, the tonsils and adenoids were removed. She had gained weight steadily and at the time of writing was considerably overweight. She had been greatly restricted in her exercise because she had continued to run a daily fever throughout this time. She had had occasional respiratory infections at which times the fever showed a higher temporary rise. At the last examination of the chest prolonged expiration to the right of the sternum in the third and fourth interspaces was present. The roentgenograms showed a gradual clearing of the ground-glass shadow in the upper lobe of the right lung. A roentgenogram taken in April, 1932, showed the interlobar fissure on the right thickened and displaced upward; the mediastinal tissues appeared to

be pulled over, and several areas of increased density were seen scattered in the right hilus and periphery.

CASE 5.—V. O., a white girl, born on Jan. 23, 1926, was admitted to the New Haven Dispensary on July 20, 1926, at the age of 6 months, because of contact with her mother, who was known to have far-advanced pulmonary tuberculosis. The infant, who had had an attack of bronchitis about one month before admission, was found to have slight fever, a positive intradermal tuberculin test (0.02 mg.) and, on roentgenographic examination, a slight increase in the width of the mediastinal shadow. Two months later the infant was admitted to the New Haven Hospital because of almost continuous slight fever, frequent vomiting and loss of weight.

On examination the temperature was 36.8 C. (98.2 F.); the weight, 5,540 Gm. The infant had moderate general glandular enlargement, purulent otitis media, enlarged red tonsils and a loose cough. Coarse rhonchi were heard in both lungs; the spleen was palpable one fingerbreadth below the costal margin. A roentgenogram taken about one week after admission showed an increase in the width of the mediastinum and an area of increased density extending into the upper part of the left lung.

During the stay in the hospital the patient was kept in bed. The temperature was normal except for occasional short febrile periods caused apparently by infections of the upper respiratory tract. About one month after admission the percussion note was found to be impaired on each side of the sternum, and two weeks later tubercle bacilli were demonstrated in the gastric contents. The appetite was poor and the gain in weight very slow. She received a high caloric diet and cod liver oil, ultraviolet irradiation or direct exposure to sunlight daily and several transfusions of blood. On April 5, 1927, the adenoids and tonsils were removed. On Aug. 12, 1927, thirteen months after a diagnosis of pulmonary tuberculosis was made, she was discharged. During the entire period of nearly one year she gained 6½ pounds (2,954.3 Gm.). She was last seen on July 3, 1931, at the age of 4½ years. She weighed 34¾ pounds (15,762.4 Gm.) and measured 39¼ inches (99.7 cm.) in height. Physical examination gave negative results except for dulness about 1.5 cm. on each side of the midsternum. A roentgenogram taken on Jan. 14, 1931, showed calcified nodules in the upper left hilus. well seen in an oblique view; the parenchyma of the lungs appeared clear.

CASE 6.—W. C., a colored boy, born on Sept. 2, 1926, was admitted to the New Haven Hospital on June 11, 1927, at the age of 9 months, because of cough and loss of weight. He was exposed when 5 months of age to a cousin who died of pulmonary tuberculosis one month before admission of the infant. He had not been well since early winter, having had repeated colds with cough and fever. Recently loss of weight, restlessness at night and wheezy respirations had been noted. The appetite had been good, and there had been no vomiting or diarrhea.

On examination the temperature was 37.2 C. (98.8 F.); the weight, 5,860 Gm. The infant was poorly nourished and had a feeble cry. A general glandular enlargement was present; there was a mucopurulent discharge from the nose; the tonsils were red. The right side of the chest expanded better than the left; the percussion note was impaired at the apex of the right lung and over the entire left side of the back and axilla; râles were heard over the right side of the chest; the breath sounds were markedly diminished over the left side of the chest with high-pitched bronchial breathing and occasional fine râles heard at the angle of the left scapula. The liver was palpable two fingerbreadths, and the spleen three fingerbreadths, below the costal margin. The extremities were emaciated, and

the muscular development was poor. The tuberculin test (0.02 mg.) was positive. A roentgenogram showed bilateral bronchopneumonia and fluid at the base of the left lung. A diagnosis of pulmonary tuberculosis and pleurisy with effusion was made.

The temperature was usually normal, with occasional rises to 38 C. (100.4 F.) or a little above. Acid-fast organisms were found in the gastric contents, although one examination of sputum gave negative results. Typical tuberculids of the skin appeared a few days after admission. Signs of peritonitis developed. A lumbar puncture gave negative results. The infant received a high caloric diet, cod liver oil, ultraviolet irradiation and direct exposure to the sun. After eight months in the hospital he was discharged to a sanatorium. The total gain in weight was 4¼ pounds (2,041 Gm.). In spite of prolonged treatment the cough persisted. At the time of discharge there were impaired resonance at the base of the left lung and the apex of the right lung and diminished breath sounds at the base of the left lung. A roentgenogram taken two weeks before discharge showed a dense area in the upper right part of the chest, a well outlined transverse fissure, a mottled increased density of the left lung and a line of pleural reflection from the fifth rib to the base. In September, 1928, the patient was readmitted to the New Haven Hospital; the diagnosis was pulmonary tuberculosis and tuberculous osteomyelitis of the spine. A roentgenogram taken at this time showed diffuse miliary infiltration of the entire right pulmonary field, slight atelectasis of the left lung and extensive calcification of the pleura. The spine showed a deformity of the first and second lumbar vertebrae. Frequent respiratory infections occurred, accompanied by fever and vomiting; the signs in the lungs remained essentially the same as on admission. In March, 1929, suppurative otitis media, mastoiditis and cervical adenitis developed. One year later (March, 1930) he had attacks of severe paroxysmal coughing. A roentgenogram taken at this time showed the pulmonary fields to be studded with small calcified nodules and increased density in the upper right pulmonary field. In January, 1932, the patient was discharged to a sanatorium.

Case 7.—J. D., a white boy, born on May 7, 1925, was admitted to New Haven Dispensary on March 31, 1927, at the age of 22 months, because his mother, who was 26 years old, was known to have advanced pulmonary tuberculosis, although her sputum had been negative on two examinations. On examination the infant had a positive intradermal tuberculin test (0.02 mg.), and a roentgenogram, which cannot be reread, was said to show the lungs in general "fairly clear throughout." Because his mother was ill he was not carefully observed, and it was not until three months later that a cough was noted. In November, 1927, at the age of 30 months, he was admitted to the New Haven Hospital. A diagnosis of pleural effusion was made. A roentgenogram confirmed this diagnosis and showed parenchymal involvement as well.

On examination the temperature was 37.8 C. (100 F.); the weight, 25½ pounds (11,566.8 Gm.), and the height, 86 cm. The infant was well developed and well nourished, but somewhat listless. The posterior cervical nodes on the right side were slightly enlarged; the tonsils were small. The right side of the thorax seemed larger than the left and moved less with respiration. The chest was resonant over the left side and at the apex of the right lung, back and front, to the fourth rib. Below this point, over the entire right side of the back, the percussion note was impaired, increasing to flatness at the extreme base. The breath sounds over this area were diminished and bronchovesicular, and numerous râles were heard. The heart was not displaced; the spleen was not felt. A roent-

genogram showed a shadow interpreted as fluid in the right pleural cavity. A thoracentesis was performed, and 25 cc. of thin straw-colored fluid was obtained, which, when inoculated into a guinea-pig, gave a positive test for tuberculosis. The gastric contents, examined during fasting on one occasion about one month after admission, showed no tubercle bacilli.

The boy was given a high caloric diet, cod liver oil and daily ultraviolet irradiation. The pulmonary signs and the appearance of the roentgenograms showed gradual improvement. Thoracentesis was not repeated. The temperature showed an occasional rise to 38 C. (100.4 F.) or slightly above, but was normal most of the time. The appetite was poor, and the patient gained only 1 pound (453.6 Gm.) during the twenty-one weeks in the hospital. He was discharged to a sanatorium on March 30, 1928. He remained in the sanatorium for about five months. On his return, although his general condition was good, the breath sounds were found to be still diminished over the right side, and occasional coarse râles were heard. Three months later he was going to school and gaining weight. Examination of the lungs gave negative results except for slight parasternal dulness. The last roentgenogram, taken on July 21, 1930, at the age of 5 years, showed a broad mediastinum and an area in the midzone at the base of the right lung which was probably a partially calcified nodule, the view of which was somewhat obscured because of the superimposed shadow of the rib. The pulmonary fields had a generalized ground-glass appearance, which was most marked opposite the left hilus and along the left bronchus, which appeared to be dilated.

TUBERCULOSIS

III. PHLYCTENULAR CONJUNCTIVITIS; ITS RELATION TO TUBERCULOSIS AS SHOWN BY ROENTGENOLOGIC AND CLINICAL OBSERVATIONS IN SEVENTY-ONE CASES

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In the pediatric and ophthalmologic literature of the past twenty years one finds many references to phlyctenular conjunctivitis. A review of this work shows that although the clinical picture is clearly recognized and varied plans of therapy are suggested, there is still no absolute agreement as to the etiology. In 1925 Aland [1] reviewed the literature on phlyctenular conjunctivitis and came to the conclusion that the preponderance of evidence was in favor of the etiologic rôle of tuberculosis, but that further statistical and therapeutic study was needed before this relationship could be definitely established. It is our purpose to present as additional evidence of this relationship a study of a group of children with phlyctenular conjunctivitis in whom particular attention was directed to the roentgenologic examination.

Two previous investigators have reported the results of roentgenologic examination of patients with phlyctenulosis. Weekers and Colmant [2] obtained roentgenograms of the chests of 50 patients subject to phlyctenulosis. Of these, 34 were children with phlyctenules at the time of examination, 2 were children who had had a previous phlyctenular attack, 3 were adults with phlyctenules, and 11 were adults who had had phlyctenules in childhood. The criterion used for division of the films into tuberculous and nontuberculous groups was the degree of enlarge-

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1. Aland, A. H.: Etiology and Pathology of Phlyctenular Keratoconjunctivitis, Am. J. Ophth. **8**:948, 1925.

2. Weekers, L., and Colmant, Y.: Phlyctènes oculaires et adénopathie trachéobronchique, Arch. d'opht. **39**:65, 1922.

ment of the mediastinal shadow. Three degrees of hilar enlargement were recognized. The first group comprised those films in which the mediastinal enlargement was slight, and these were considered as being nontuberculous. The second group comprised those in which there was pronounced mediastinal enlargement, and these were considered as representative of active tuberculous tracheobronchial lymphadenitis. The third group comprised those in which, in addition to enlargement of the mediastinum, there were definite calcific deposits. Of the 50 films examined, none fell in the first group; those of 36 children and 11 adults were in the second group, and those of 3 adults were in the third group. In a control group of 10 children there were 3 with negative films and 7 with findings classified as first degree. Weekers and Colmant concluded that the appearance of phlyctenules indicates the presence of tuberculous tracheobronchial nodes in activity. They felt, however, that the roentgen findings should always be interpreted in conjunction with the clinical examination.

Stalder [3] examined fluoroscopically 100 patients with phlyctenulosis. Of these, 83 showed definite hilar enlargement, 11 had doubtful signs, and only 6 definitely had no enlargement. Of the 83 cases grouped as positive, 19 showed calcium. The author felt that the number of cases in which there were positive findings would have been even greater had the observations extended over a longer period. Enlargement of the hilus was a typical finding before the fifth year of life; after that there was usually evidence of calcification. Physical signs of tuberculosis were more frequent in patients past the age of 16. He also felt that the appearance of phlyctenules in a person with hilar roentgen findings indicates activity of the tuberculous process.

In both of the studies just summarized, however, the examination was limited to the thorax. Weekers and Colmant obtained only anteroposterior views, and Stalder's study consisted of a single fluoroscopic examination. The basis of classification seems unsatisfatory in view of the results of recent studies of tuberculosis in children in which large numbers of roentgen examinations have been carried out. These studies have pointed out the value of roentgen examination of the neck, chest and abdomen, and have stressed the necessity of careful standards of comparison in interpretation of films of the chest taken solely in the anteroposterior position.

ETIOLOGY

We do not intend to report in detail the etiologic theories that have been suggested for phlyctenulosis. Among these are bad living condi-

3. Stalder, H.: Zur Kenntnis der Lungenbefunde bei Augenskrophulose, Schweiz. med. Wchnschr. **56**:618, 1926.

tions,[4] errors of refraction,[5] eczema,[6] autointoxication,[7] diseased tonsils and adenoids,[8] herpes,[9] acne rosacea,[10] pediculosis,[11] ethmoiditis,[12] anaphylaxis [13] and enlargement of the carbohydrate metabolism.[14] Reviews of these various theories will be found in the articles of Aland, Gibson,[15] Trattner [16] and Knorr and Maldeis.[17] In general, however, most authors are in accord in viewing phlyctenulosis as a focal manifestation of a systemic disease, and such a concept would naturally direct attention to tuberculosis as a possibility. But any discussion of phlyctenulosis as a manifestation of tuberculous infection must consider the frequency of this disease of the eye in scrofula. Whether or not one views all the signs of scrofula as of tuberculous origin, it is evident that before the discovery of the tubercle bacillus and the subsequent increase in knowledge of the disease, phlyctenulosis was recognized as a frequent symptom in scrofulous children. Beer [18] gave the name "ophthalmia externa scrofulosa" to the disease in 1813, and this relationship was generally stressed throughout the nineteenth century. Later, however,

4. Savin, L. H., and Preston, T. W.: The Problem of the Phlyctenular Child, Lancet **1**:965, 1925.

5. Eyre, J. W.: Tuberculosis of the Conjunctiva: Its Etiology, Pathology and Diagnosis, Lancet **1**:1319, 1912.

6. Theobald, S.: The Etiology of Phlyctenular Ophthalmia, J. A. M. A. **63**: 566 (Aug. 15) 1914.

7. Columbo, G. L.: Ueber die Pathogenese der ekzematösen Keratokonjunktivitis (skrofulösen), Klin. Monatsbl. f. Augenh. **49**:164, 1911; Die Autodarmintoxikation in der Pathogenese der ekzematösen Keratokonjunktivitis, ibid. **50**: 610, 1912.

8. Kirkendall, J. S.: Infectious Phlyctenular Kerto-Conjunctivitis, New York State J. Med. **9**:164, 1909. Milne, G.: Phlyctenular Conjunctivitis and Adenoids, Brit. J. Ophth. **3**:163, 1918. Savin and Preston.[4]

9. Bruns, H. D.: Phlyctenular Ophthalmia and Its Etiology, J. A. M. A. **59**:1002 (Sept. 21) 1912.

10. Peters, A.: Remarks on Rosacea of the Eye, Ztschr. f. Augenh. **69**: 144, 1929; abstr., Am. J. Ophth. **13**:358, 1930.

11. Laurell, H.: Phlyctenular Conjunctivitis and Scrofulosis, Upsala läkaref. förh. **31**:711, 1926; abstr., J. A. M. A. **87**:2136 (Dec. 18) 1926.

12. Turner, H. H.: Etiology of Phlyctenular Ophthalmia, Am. J. Ophth. **3**: 115, 1919.

13. Funaishi, S.: Treatment of Phlyctenular Inflammations of the Eye, Am. J. Ophth. **8**:618, 1925.

14. Goldenburg, M.: The Pathogenesis of Ophthalmia Eczematosa, J. A. M. A. **69**:104 (July 14) 1917.

15. Gibson, W. S.: The Etiology of Phlyctenular Conjunctivitis, Am. J. Dis. Child. **15**:81 (Feb.) 1918.

16. Trattner, S.: Phlyctenular Kerato-Conjunctivitis, Virginia M. Monthly **50**:117, 1923.

17. Knorr, E. A., and Maldeis, H. J.: Etiology of Phlyctenular Conjunctivitis, Maryland M. J. **56**:90, 1913.

18. Beer, cited by Knorr and Maldeis.[17]

with the demonstration of the tubercle bacillus as the cause of a great part of the symptomatology of scrofula, the term became less and less frequent in usage, so that today—in this country at any rate—it is rarely used. The development of the reaction to tuberculin and the high incidence of positive reactions in scrofulous children also enhanced the general acceptance of the relationship between scrofula and tuberculosis. Marfan,[19] however, along with other European writers, expressed the belief that the term has a definite place in describing a particular type of child in whom a particular type of tuberculosis is apt to develop. He recognized the frequent occurrence of phlyctenules as a symptom in such children. It was partly in an attempt to explain the relationship between scrofula and tuberculosis that Czerny propounded the doctrine of the exudative diathesis.

The premise that tuberculosis—either of the usual or of a special type—is the underlying factor in the production of phlyctenules has led to a study of the problem on histologic, experimental, clinical and therapeutic bases. Histologically, the phlyctenule, while not a true tubercle, resembles certain forms of tuberculous tissue. The most exact descriptions of the microscopic anatomy of the phlyctenule in human beings are found in the papers of Weekers [20] and Hayashi,[21] who excised phlyctenules for microscopic study. Weekers examined 25 phlyctenules, and Hayashi 11. The phlyctenule consists of a collection of cells lying just beneath the conjunctival epithelium, and in corneal cases just beneath Bowman's membrane. In the early stages the cells are predominantly polymorphonuclear leukocytes, but later these cells are replaced by small lymphocytes. Among the lymphocytes are seen a few epithelioid cells with large pale nuclei, and occasionally a few multinucleated cells are present. In the latter the number of nuclei is never large, and the giant cell of Langhans' type is never seen. The epithelium itself is involved in the process, as is shown by thinning and degeneration of some of the cells. The surrounding capillaries are distended and show endothelial proliferation. Tubercle bacilli, true giant cells or caseation is not observed. These findings have been substantiated by histologic study of phlyctenules experimentally produced by various investigators.

Weekers [22] produced phlyctenules in tuberculous rabbits by repeated instillations of tuberculin into the conjunctival sac. The same procedure failed to produce conjunctival lesions in nontuberculous animals.

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19. Marfan, A. B.: Scrofule et ophtalmie phlycténulaire, Presse méd. **36**: 1105, 1928.

20. Weekers, L.: Anatomie pathologique des phlyctènes oculaires, Bull. Acad. roy. de méd. de Belgique **24**:455, 1910; cited by Gibson [15] and by Weekers.[22]

21. Hayashi, M.: Beiträge zur pathologischen Anatomie der Phlyktäne und phlyktäneähnlicher Prozesse, Klin. Monatsbl. f. Augenh. **47**:557, 1909.

22. Weekers, L.: Phlyctènes oculaires et tuberculose, Arch. d'opht. **44**:342 and 411, 1927.

Rosenhauch [23] then produced phlyctenules by the same method, but also produced them in tuberculous animals by instilling staphylococcus toxin into the eyes. He concluded that a number of external local irritants could produce phlyctenules in tuberculous animals. Rubert,[24] in an extended series of experiments, repeated the observations of Weekers and Rosenhauch with tuberculin, and also produced them in a few instances with staphlylococcus toxin. He went further, however, by subjecting nontuberculous animals to repeated injections of tuberculin subcutaneously, and subsequently dropped tuberculin into the eyes. In one instance a nodule resembling a phlyctenule appeared. Gibson [15] has also successfully produced phlyctenules. In his experiments he used many variants, but like the others was able to produce the nodules only in tuberculous animals. He obtained them six times with the local use of tuberculin and twice with no local irritation whatsoever, but could not repeat Rosenhauch's experience with staphlylococcus toxin. Guillery [25] recently has adopted a new approach to the problem. He felt that the majority of experimental phlyctenules differed from those occurring spontaneously in human beings in that in the production of the former local irritation was always the method used. He then devised a rather ingenious method of tying into various parts of the animal body—sometimes remote from the eye—little sacs of tubercle bacilli arranged in such a manner that the body fluids could get in and toxins could get out, yet the bacilli themselves were held localized. Having thus reproduced conditions as they are found in human beings, he found that phlyctenules appeared regularly in these animals without resort to local irritation of any form. He made careful histologic studies of his results, and strongly advocated microscopic study of the whole eye if a clear understanding of the process is desired. Besides the evident phlyctenule in these eyes he found that practically all of the vessels of the eye are distended, and along many of them he found collections of cells strung out in longitudinal fashion. Because of the relatively copious supply of blood around the limbus the process is more marked in this locality. He expressed the belief that there are clinical and subclinical forms of phlyctenulosis, and that in many cases the subclinical form is transformed into the clinically evident form by local irritation. Thus it is, he said, that various toxins, irritants and even the rubbing and scratching attendant on pediculosis have been considered as the causative agents. He expressed the opinion that the true phlyctenule is always a tuberculotoxic manifestation.

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23. Rosenhauch, E.: Ueber das Verhältnis phlyktänulären Augenentzündungen zur Tuberkulose, Arch. f. Ophth. **86**:371, 1910.

24. Rubert, J.: Ueber die Aetiologie der phlyctänulären Augenentzündung, Klin. Monatsbl. f. Augenh. **50**:273, 1912.

25. Guillery, H.: Die Phlyktäne und andere Erscheinungen der Skrofulose als tuberkulotoxische Erkrankungen, Virchows Arch. f. path. Anat. **273**:806, 1929.

But the greatest bulk of evidence in favor of underlying tuberculous infection as the cause of phlyctenulosis has come from the clinical study of groups of children with this form of conjunctivitis. The strikingly high incidence of positive reactions to tuberculin, the frequent association of other tuberculous lesions and positive family histories, the occasional flare-up of the local condition after a test of the skin with tuberculin, the appearance of phlyctenules during the course of a positive ocular reaction to tuberculin and the beneficial therapeutic results obtained with tuberculin by some authors have strongly suggested this relationship. Stephenson and Jamieson [26] found a positive Pirquet reaction in 20 children between the ages of 2 and 12 years with phlyctenulosis. Of these patients, 50 per cent showed physical signs of tuberculosis, and 75 per cent gave a family history of tuberculosis. Tivnen [27] found a positive Pirquet reaction in 46 of 50 cases, a positive family history in 10, and in 4 cases an exacerbation of the ocular condition following the test of the skin. He also obtained satisfactory results with therapeutic injections of tuberculin. Davis and Vaugan [28] studied 40 cases and found a positive Pirquet reaction in 70 per cent, a positive family history in 17.5 per cent and a focal reaction in 7 per cent. They too obtained satisfactory results with tuberculin therapeutically. Belenky-Raskin [29] found a positive Pirquet reaction in 90 of 100 cases, and of the 10 negative reactors, 8 had positive family histories or physical signs of tuberculosis. Goldbach [30] studied a group of 39 children and found that 32 had a positive Pirquet reaction, 7 had pulmonary tuberculosis, and 16 had some other demonstrable form of tuberculous infection. Gibson [15] reported the results of careful and detailed examination of 92 children with phlyctenulosis. Of these, 90 had a positive reaction to the Pirquet test, many of them being strongly positive reactions, and in the 2 cases in which negative reactions were obtained the diagnosis of the conjunctival lesion was not absolutely certain. Of these children, 40 were under the age of 5 years, and all but 1 reacted positively. There had been direct exposure to tuberculosis in 29 per cent of the children, and in 26 per cent there were clinical signs of tuberculous infection. Careful examination and histories revealed no

26. Stephenson, S., and Jamieson, J.: A Note Upon Phlyctenular Affections of the Eye, Brit. M. J. **1**:916, 1910.

27. Tivnen, R. J.: Tuberculin as a Diagnostic and Therapeutic Agent in the Treatment of Conjunctivitis Eczematosa, J. A. M. A. **57**:1886 (Dec. 9) 1911.

28. Davis, E. A., and Vaugan, H.: Phlyctenular Conjunctivitis and Keratitis, with Special Reference to Etiology and the Value of Tuberculin as a Diagnostic Agent, Ophth. Rec. **21**:476, 1912.

29. Belenky-Raskin: Zur Aetiologie der phlyktänulären Augenentzündung, Ztschr. f. Augenh. **29**:503, 1913.

30. Goldbach, L. J.: Lymphatic-Nodular Keratoconjunctivitis (Phlyctenules), J. A. M. A. **69**:102 (July 14) 1917.

other single factor in a large enough percentage of the cases to be considered as playing an etiologic rôle. Gibson believed that tuberculosis was always the cause of phlyctenulosis. Casparis [31] reported excellent results with tuberculin therapy, and also expressed a belief in the presence of underlying tuberculosis in every case of phlyctenulosis. Trattner [16] has summarized the results of the tuberculin test in these children as found by eleven different authors. Of 903 cases, the tuberculin test was positive in 769, or 85 per cent. In three series of children under 6 years of age without phlyctenulosis, totaling 1,806 cases, positive reactions were obtained in 18.8 per cent; whereas in three series of phlyctenular children under 6, totaling 118 cases, positive reactions were obtained in 90 per cent. These results, in conjunction with his own observations on phlyctenular children, have led Weekers [22] to suggest the mechanism of the production of phlyctenules as a tuberculotoxic manifestation. He expressed the belief that phlyctenules develop in persons who present an extreme hypersensitivity to tuberculin. Between the ages of 1 and 15 years, the majority of the population acquires tuberculous infection, and hence becomes allergic to tuberculin. During the same age period phlyctenules develop in certain persons. The latter group, he believed, consists of those persons in whom the first processes of infection and immunity are initiated in a manner which exceeds the normal. The tissues of the body, including the conjunctiva, become extremely hypersensitive to tuberculin. Subsequently, infinitesimal amounts of tuberculin carried from an endogenous source by the blood and thence to the eye by the tears are capable of evoking a response on the part of the hypersensitive conjunctiva. This response is characteristically in the form of the phlyctenule. Thus Weekers concluded that the appearance of phlyctenules indicates the presence of an active focus of tuberculosis, usually situated in the tracheobronchial nodes. Guillery [25] stressed the rôle of underlying tuberculous infection, but expressed the opinion that varied forms of local irritation are capable of evoking phlyctenules in the altered or hypersensitive conjunctiva.

PRESENTATION OF DATA

We have examined 71 children with phlyctenulosis. The majority of these children were admitted to the clinic for diseases of the eyes of the New Haven Dispensary because of the local condition.[32] When the diagnosis was made, they were referred to the special clinic maintained

31. Casparis, H.: Phlyctenular Keratoconjunctivitis: Its Etiology and Treatment, Am. J. Dis. Child. **34**:779 (Nov.) 1927.

32. Dr. Eugene Blake and Dr. Arthur Yudkin cooperated in the examinations of the eyes. Dr. Jesse Harris and the late Dr. A. M. Wakeman made many of the clinical observations.

for the study of tuberculosis in childhood,[33] where a history, physical examination, roentgen examination and tuberculin test, when permitted, were obtained. The results of these examinations are summarized in table 1.

The children ranged from 10 months to 12 years of age. There were 9 children under 2 years of age, 42 children between the ages of 2 and 6 years, and 20 children over 6 years.

In the 60 cases in which tuberculin tests were performed there were 58, or 96.6 per cent, positive reactions and only 2 negative reactions.

Physical evidence of tuberculosis was found in 21 children, or 30 per cent of the total number.

A history of contact with tuberculosis was elicited in 33 cases, or 46.4 per cent of the total number.

In all of the children the roentgenographic series consisted in examination of the neck, chest and abdomen, and in a few special cases plates

TABLE 1.—*Summary of Clinical Observations on Seventy-one Children with Phlyctenulosis*

Roentgen Classification	Number	Tuberculin Test			Contact History		Physical Examination	
		Positive	Negative	Not Done	Positive	Negative	Positive	Negative
Positive	48	41	0	7	25	23	18	30
Suggestive	13	10	1	2	5	8	1	12
Negative	10	7	1	2	3	7	2	8
Total	71	58	2	11	33	38	21	50

of particular bones were taken as indicated. It will be seen that 48, or 67.6 per cent, of the roentgenograms were definitely positive for signs of tuberculosis, 13, or 18.3 per cent, were suggestive, and 10, or 14 per cent, were classified as negative. The roentgenograms were classified after careful consideration, and only those which showed definite calcification in the neck, chest or abdomen, pulmonary infiltration or definite changes in the bones were placed in the positive group. Plates in which the mediastinum was enlarged and "fluffy" in appearance but in which there was no definite calcification were classified as suggestive. The negative group comprised those plates which seemed normal, those which were technically not satisfactory, and those in which the degree of mediastinal thickening was no greater than we have frequently seen accompanying various infections of the respiratory tract. We should like to stress here that the classification given here-

33. The purpose of this clinic is to follow up children in whom there is reason to suspect that tuberculous infection has occurred or is likely to occur. By far the largest number consists of known contacts, but there are many referred for study because of positive tuberculin tests or suggestive physical findings. In some of the latter groups it has been impossible to establish definite contact.

with is based solely on the appearance of the film itself, and we believe that most of the suggestive cases and many of the negative ones, if considered in conjunction with the clinical observations, would fall into the positive group. A child with a history of exposure, a positive tuberculin test and a suggestive mediastinum on roentgen examination would ordinarily be treated as tuberculous. The frequency of the various types of positive roentgen findings in relation to age is seen in table 2.

The most common finding was tuberculosis of the tracheobronchial glands. This was seen in 24 instances, and was associated with the presence of a primary nodule in 9 films and with mesenteric lymphadenitis in 1. Primary nodules were visible in 12 roentgenograms. Calcified abdominal glands were seen in 19 films. They were the only

TABLE 2.—*Summary of Positive Roentgen Findings, the Cases Being Grouped According to Age*

Age Groups	Number Examined	Tuberculosis of Tracheobronchial Glands	Primary Nodules	Tuberculosis of Mesenteric Glands	Tuberculosis of Cervical Glands	Pulmonary Infiltration	Bones (Spine)
Under 2.....	4	1	2 (1*)	2	0	0	0
2 to 6.....	34	16	5 (4*)	14 (1*, 2†, 1‡)	4	1	2
Over 6.....	10	7	5 (4*)	3 (1*)	0	0	0
Total.....	48	24	12	19	4	1	2

* The number also showing calcium in the tracheobronchial glands.
† The number also showing calcium in the cervical glands.
‡ The number also showing a primary nodule.

roentgen evidence of tuberculosis in 14 instances, and were associated with calcified tracheobronchial nodes once, with a primary nodule once and with calcified cervical nodes twice. There were 4 examples of calcified cervical glands and 2 examples of tuberculosis of the bone, and 1 film showed pulmonary infiltration which on later films proved to be tuberculous.

COMMENT

Great advances have recently been made in the understanding of the childhood type of tuberculosis by studies of large groups of cases in which contact has occurred, especially by studies of the family and of school children as carried out by Opie and his co-workers.[34] This work

34. (*a*) Opie, E. L., and McPhedran, F. M.: The Contagion of Tuberculosis, Am. Rev. Tuberc. **14**:347, 1926. (*b*) Opie, E. L.; Landis, H. R. M.; McPhedran, F. M., and Hetherington, H. W.: Tuberculosis in Public-School Children, ibid. **20**:413, 1929. (*c*) Hetherington, H. W.; McPhedran, F. M.; Landis, H. R. M., and Opie, E. L.: A Survey to Determine the Prevalence of Tuberculous Infection in School Children, ibid. **20**:421, 1929.

has served to point out the two reliable aids in diagnosis, namely, the tuberculin test and the roentgen examination. McPhedran,[35] who has been especially interested in the latter procedure, has shown the difficulties of interpretation of films taken only in the anteroposterior position, and has suggested the oblique position as an important step in arriving at the correct roentgen diagnosis. Dunham and Smythe [36] have called attention to the relative frequency of tuberculous mesenteric lymphadenitis demonstrable in roentgenograms, and in a later paper [37] have shown the value of the roentgen rays in the diagnosis of tuberculosis of the cervical lymph glands. The importance of examinations of the mesenteric and cervical glands is brought out by our series of 48 positive roentgenograms, 18, or 37.5 per cent, of which showed no evidence of tuberculosis except in one or the other of these localities.

There were 21 children, or 30 per cent of the total number, who showed evidence of tuberculous infection on physical examination. Compatible pulmonary signs (19 cases), tuberculous cervical adenitis [38] (5 cases), changes in the bones (2 cases) and tuberculids of the skin (2 cases) were taken as positive signs. The number of positive physical examinations in this group is relatively high when compared with that obtained in large groups of nonphlyctenular children with tuberculous infection as shown by roentgen examination and tuberculin tests, yet even here it is evident that without these procedures the diagnosis could not be definitely established in the majority of cases. No other single physical finding or combination of physical findings was prevalent in sufficient proportion to direct attention to a possible etiologic relationship. The incidence of a definite history of contact in 33, or 46.4 per cent, of the patients surely is suggestive of an etiologic relationship.

There can be little doubt that the percentage of positive reactors to tuberculin in groups of these children is much higher than that found for general populations of children, and this figure is even more striking when the age groups are considered. In our series 8 children under 2 years of age were tested, and 7, or 87.5 per cent, reacted. Of 35 children between the ages of 2 and 6 years, 34, or 97 per cent, reacted, and 17 children over 6 years of age reacted. There have been many

35. McPhedran, F. M.: The X-Ray Diagnosis of Pulmonary Tuberculosis in Children, Am. Rev. Tuberc. **16**:420 and 479, 1927; The Diagnosis and Classification of Pulmonary Tuberculosis in Childhood and Adolescence, ibid. **20**:532, 1929.

36. Dunham, E. C., and Smythe, A. M.: Tuberculosis of Abdominal Lymph Nodes: Diagnosis by Means of the Roentgen Ray, Am. J. Dis. Child. **31**:815 (June) 1926.

37. Dunham, E. C., and Smythe, A. M.: Tuberculosis of the Cervical Lymph Nodes in Infancy, Am. J. Dis. Child. **34**:962 (Dec.) 1927.

38. Clinically tuberculous. Three of these were proved by biopsy.

studies of the incidence of positive reactions to tuberculin in various large groups of children. A few of these results, which are summarized in table 3, will suffice to show the greater incidence in those with phlyctenulosis. Opie and McPhedran,[34a] in subjects under 5 years of age, found positive reactions in 80 per cent of children who had had contact with tuberculosis and in 23.3 per cent of those who had not. Among those between the ages of 5 and 10 years, there were positive reactions in 80.4 per cent of the children who had had contact with tuberculosis and in 35.5 per cent of those who had not. Asserson [39] and

TABLE 3.—*Incidence of Positive Reactions to Tuberculin in Various Groups of Children*

Age Spread	Source	Group	Type of Test	Number Tested	Percentage Positive
0 to 2	Present series	Phlyctenular	Mantoux*	8	87.5
	Clinic records	New Haven Dispensary Clinic for Childhood Tuberculosis	Mantoux	174	23.2
	Asserson	General Hospital	Not stated	4,003	11.4
	McLean and Jeidell	General Hospital	Pirquet	2,850	10.5
	Smith	General Hospital	Mantoux	3,495	7.5
	Asserson	Baby Clinics	Mantoux	1,656	3.0
2 to 6	Present series	Phlyctenular	Mantoux*	35	97.0
	Clinic records	New Haven Dispensary Clinic for Childhood Tuberculosis	Mantoux	704	48.8
	Opie and McPhedran†	Contact	Mantoux	15	80.0
	Opie and McPhedran†	Noncontact	Mantoux	9	23.3
	Smith	General Hospital	Mantoux	1,923	16.5
6 to 10	Present series	Phlyctenular	Mantoux*	17	100.0
	Clinic records	New Haven Dispensary Clinic for Childhood Tuberculosis	Mantoux	41	82.0
	Opie and McPhedran‡	Contact	Mantoux	92	80.4
	Opie and McPhedran‡	Noncontact	Mantoux	45	35.5
	Harrington and Myers	General school	Mantoux	1,179	38.8
	Smith	General Hospital	Mantoux	1,529	27.4

* In a few of the earlier cases Pirquet tests were made.
† Age spread, 0 to 5.
‡ Age spread 5 to 10.

McLean and Jeidell [40] have studied the incidence of positive tuberculin tests in infants under 2 years of age who were admitted to general hospitals for all reasons, including tuberculosis. Asserson found positive reactions in 11.4 per cent of 4,003 infants, and McLean and Jeidell found positive tests in 10.5 per cent of 2,850 infants. Asserson also tested 1,656 infants in various health clinics in New York City and found that only 3 per cent were positive reactors. Smith [41] tested 7,668 subjects in the children's medical service at Bellevue Hospital in New

39. Asserson, M. A.: Tuberculosis in Infants, Am. Rev. Tuberc. **16**:359, 1927.

40. McLean, S., and Jeidell, H.: Data in Three Thousand Seven Hundred and Forty-Two Pirquet Tests, Am. J. Dis. Child. **24**:73 (July) 1922.

41. Smith, C. H.: Tuberculin Skin Reactions, Am. J. Dis. Child. **38**:1137 (Dec.) 1929.

York. Using the Mantoux test, he found positive reactions in 7.5 per cent of the infants under 2 years of age, in 16.5 per cent of the children from 2 to 6 and in 27.5 per cent of those between the ages of 6 and 10. Harrington and Myers [42] found positive reactions in 38.8 per cent of Minneapolis school children between the ages of 6 and 10. In the clinic for childhood tuberculosis at the New Haven Dispensary, where the incidence of positive tuberculin tests would naturally be higher than in an unselected group of children, we found positive reactions in 44.5 per cent of approximately 1,000 children. From birth to 2 years positive tests occurred in 23.2 per cent of the total; from 2 to 6 years, in 48.8 per cent, and above the sixth year, in 82 per cent.

If the phlyctenule is considered as a manifestation of hypersensitiveness to tuberculin, those cases of the disease in which a negative tuberculin test is obtained deserve special mention. In our series there were 2 such cases. One of them was that of a boy, aged 2 years, whose roentgenograms showed a suggestive mediastinum. There was dulness at the apex of the right lung on physical examination. His mother had open pulmonary tuberculosis. In this case, however, only a single Pirquet test was permitted, and we believe that repetition of the test intradermally in stronger dilution probably would have invoked a positive reaction. The second child was first seen at the age of 18 months, when he was admitted to the New Haven Hospital because of atelectasis of a part of the lung subsequent to pneumonia. Recovery was rapid after removal of a plug of mucus from a large bronchus through a bronchoscope. The intradermal tuberculin test (0.1 mg.) was negative at this time. Three months later the child was seen in the dispensary, and a diagnosis of phlyctenular conjunctivitis was made. Roentgenograms taken at this time were negative, as were tuberculin tests up to 1 mg. In this case, however, the conjunctivitis lasted but three days, and although the child has been followed up for six years, there has been no reappearance of symptoms. Roentgenograms and tuberculin tests have been repeatedly negative during this period. It will be agreed that the clinical course in this case is different from that of the chronic, recurrent type of phlyctenular disease in scrofulous children, and it is this type of case that has led Hansell,[43] Alexander [44] and others to question the statement that all phlyctenules have a tuberculous background. The explanation for such cases is difficult; yet it seems that it may lie in the question of correct diagnosis of the lesion

42. Harrington, F. E., and Myers, J. A.: Studies on Tuberculosis in Infancy and Childhood, Am. Rev. Tuberc. **14**:454, 1926.

43. Hansell, H. F.: A Consideration of the Etiology of Phlyctenular Disease of the Eye, Am. J. Dis. Child. **16**:262 (Oct.) 1918.

44. Alexander, L. W.: Some Recent Observations in Phlyctenular Diseases, South. M. J. **24**:384, 1931.

of the eye. In Gibson's [15] series the conjunctivitis was not absolutely typical in the 2 children who did not react to tuberculin. It may be, then, that there is a relatively uncommon form of conjunctivitis which at the onset closely resembles the phlyctenule, but which does not have the typical chronic course manifested by the latter. Guillery [25] recognized such occurrences, and expressed the belief that careful histologic examination, if possible, would reveal differences in structure between this type of lesion and the more common tuberculotoxic phlyctenule.

SUMMARY

1. It is generally recognized through anatomic, experimental and clinical studies that tuberculosis bears an etiologic relationship to phlyctenular conjunctivitis.

2. Study of a group of 71 children from 10 months to 12 years of age with phlyctenulosis revealed positive roentgen evidence of tuberculosis in 48 (67.6 per cent), suggestive roentgenograms for 13 (18.3 per cent) and negative films for 10 (14 per cent). Tuberculin tests yielded positive results in 58 of 60 children tested (96.6 per cent). There was a positive history of contact with tuberculosis in 33 cases (46.4 per cent), and physical signs of tuberculosis were present in 21 (30 per cent). No other single condition was found in a proportion large enough to suggest an etiologic rôle.

3. The importance of roentgenographic examination of the neck and abdomen is substantiated by the present series of phlyctenular children. The only roentgen evidence of tuberculosis was found in the neck and abdomen in 18 instances, 37.5 per cent of the total of 48 positive roentgenograms.

4. It is possible that there is a relatively uncommon form of conjunctivitis clinically difficult at the onset to distinguish from tuberculous phlyctenulosis, which is caused by some other factor; but in the vast majority of cases of phlyctenular conjunctivitis careful study will reveal the presence of underlying tuberculous infection. This study should include, in addition to the history, physical examination and tuberculin test, a roentgenologic examination of the neck, chest and abdomen.

Pediatric Biographies

JOHN CLARKE
1761-1815

JOHN RUHRÄH, M.D.
BALTIMORE

John Clarke, son of a surgeon of the same name, was born at Wellingsborough, Northamptonshire, England, in 1761. At 11 years of age he was sent to St. Paul's school. He attended lectures by the two Hunters and George Fordyce and was a student at St. George's Hospital. The barbers had by that time been separated from the surgeons, and he joined the corporation of surgeons, as the body had not yet reached the dignity of a college. He began practice in Chancery Lane and also to lecture on midwifery in the private medical school of William Hunter. In 1787 he received a license in midwifery from the College of Physicians and removed to the west end. He received a degree from some Scotch University about 1791. He lectured on midwifery at St. Bartholomew's Hospital and was one of the best known practitioners of obstetrics in London, but later gave up that work and confined himself to consultations on women's and children's diseases. He died in August, 1815, from some "organic disease of the stomach and ascites."

His publications, besides a paper on tumors of the placenta, consist of three volumes: "An Essay on the Epidemic Diseases of Lying-in Women in 1787-1788," London, 1788; "Practical Essays on Pregnancy and Labour and the Diseases of Lying-in Women," London, 1793, and the posthumously printed "Commentaries on Some of the Most Important Diseases of Infants and Children," London, 1815.

This last is in some ways a remarkable work containing as it does a clear account of tetany and laryngismus stridulus. Laryngismus stridulus was confused by Boerhaave with asthma and is sometimes even today mistaken for croup or laryngitis.

ON A PECULIAR SPECIES OF CONVULSION IN INFANT CHILDREN

There is one case of convulsive affection, which is more apt to be overlooked than any other, because the symptoms are not at first very violent, so as to attract the attention of parents or nurses. It is often mistaken and treated as some other disease, even by medical men; and the true character of it has been little known, even to practitioners generally conversant with infantile disorders; it is therefore less likely to be detected by those who have bestowed little or no attention upon them.

This convulsive affection occurs by paroxysms, with longer or shorter intervals between them, and of longer or shorter duration in different cases, and in the same case at different times.

It consists in a peculiar mode of inspiration, which it is difficult accurately to describe.

The child having had no apparent warning, is suddenly seized with a spasmodic inspiration, consisting of distinct attempts to fill the chest, between each of which a squeaking noise is often made; the eyes stare, and the child is evidently in great distress; the face and the extremities, if the paroxysm continues long,

COMMENTARIES

ON SOME OF THE

MOST IMPORTANT

DISEASES OF CHILDREN.

BY

JOHN CLARKE, Esq. M.D.

&c. &c. &c.

PART THE FIRST.

54647

LONDON:

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1815.

Title page from John Clarke's book on children.

become purple, the head is thrown backward, and the spine is often bent, as in opisthotonos; at length a strong expiration takes place, a fit of crying generally succeeds, and the child, evidently much exhausted, often falls asleep.

In one of these attacks a child sometimes, but not frequently, dies.

They usually occur many times in the course of the day, and are often brought on by straining, by exercise, and by fretting, and sometimes they come on from no apparent cause.

They very commonly take place after a full meal, and they often occur immediately upon waking from sleep, though before the time of waking the child had been lying in a most tranquil state. As the breathing is affected by these paroxysms, the complaint is generally referred to the organs of respiration, and

it has been sometimes called chronic croup; but it is very different from croup; and is altogether of a convulsive character, arising from the same causes, and is relieved by the same remedies as other convulsive affections.

Accompanying these symptoms, a bending of the toes downwards, clenching of the fists and the insertion of the thumbs into the palm of the hands, and bending the fingers upon them, is sometimes found, not only during the paroxysm, but at other times.

Clenching the fist with the thumb inserted into the palm of the hand, often exists for a long time in children, without being much observed, yet it is always to be considered as an unfavourable symptom, and frequently is a forerunner of convulsive disorders, being itself a spasmodic affection.

It rarely happens that a child recovers from an attack of this sort, unless the progress of the disorder has been interrupted by a timely application of proper remedies, without a general convulsion. Then the friends become alarmed, and a disease, which had existed for two or three months, is for the first time considered to be important enough to require medical assistance, after all the farago of popular medicines, such as fit drops, soot drops, asafoetida, etc., have been ineffectively applied.

Convulsions of this description seldom, if ever, occur after the expiration of the third year of a child's life, and not often in children which have lived by sucking, till they have teeth, and have never taken animal food till the dentes cuspidati have come through the gums; this, however, is liable to some exception.

A long and very attentive consideration of this kind of convulsion, has led the writer to conclude, that in every case of convulsion (be the remote cause whatsoever it may) the brain is at the time organically affected, either directly or indirectly; directly when convulsions arise from phrenitis, hydrocephalus, or on the sudden retiring of cutaneous eruptions, or of inflammation of the mucous membrane of the eyelids and eyes, or when they appear on the accession of some cutaneous disease, attended with febrile symptoms, especially scarlet fever, smallpox, and (sometimes, though less frequently), of measles: indirectly, as when they are occasioned by an overloaded stomach or by indigestion, by peripneumony, by inflammation, or suppuration in the cavity of the pericardium, by glandular or other humors pressing on the large vessels leading to the lower extremities, or when they take place in the progress of infantile fever, or in marasmus.

Pediatrics in Art

QUADRUPLETS

JOHN RUHRÄH, M.D
BALTIMORE

An unknown painter, of the Oberdeutsch school, about 1450 painted a lying-in scene which now hangs in the Lichtenstein Palace in Vienna. Some state that it recounts an old legend of a saint, but

Lying-in scene depicting new-born quadruplets.

I have not been able to locate it. The saint is seen in the picture giving his blessing with a most correct gesture. Perhaps he thought a woman with quadruplets would need it. Three of the children already swathed lie on the bed, while the mother hands the last naked child to the midwife. The cradle stands to one side, and it is evident that the arrival of four was not expected. There is a tub for bathing the children, and the midwife's kit lies open, showing some binders. The

bed is interesting as it has a short baldachin after the manner of the beds found in the Tyrol. A picture of interest in this connection is one painted by some Dutch artist showing a lying-in room of a woman who had just given birth to quintuplets, four living and one dead. This was an actual occurrence in Scheveningen in 1719, and the artist painted the portraits of the mother and midwife, whom he names, and also of all the visitors.

News and Comment

CLEVELAND SESSION—AMERICAN MEDICAL ASSOCIATION

Scientific Exhibit

The Section on Pediatrics of the American Medical Association will sponsor a section exhibit in the Scientific Exhibit at the Cleveland Session, June 11-15, 1934. The section exhibit committee is composed of: F. Thomas Mitchell, chairman, Memphis, Tenn., W. C. Fargo, Cleveland, and A. Levinson, Chicago.

Applications for space will close on Feb. 26, 1934. Application blanks may be obtained from the members of the committee or from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago.

SOCIETY NEWS

American Orthopsychiatric Association.—The eleventh annual meeting of this association will be held at the Palmer House in Chicago, on Feb. 22, 23 and 24, 1934. Dr. Phyllis Bartelme is the chairman of the committee on arrangements.

DEATHS

Dr. Dyonis Pospischill, the eminent pediatrician of Vienna, Austria, died on Oct. 28, 1933, at the age of 65. Dr. Pospischill had for many years been in charge of the Wilhelminen-Spital, Infectious Pavilion, and had contributed much to the knowledge of contagious diseases in children. His loss will be greatly felt.

Correspondence

PATHOGENESIS OF ATELECTASIS OF THE NEW-BORN

To the Editor:—In a recent paper on "Pathogenesis of Atelectasis of the New-Born" in the AMERICAN JOURNAL OF DISEASES OF CHILDREN (**46**:590 [Sept.] 1933) by J. L. Wilson and Sidney Farber, a conception of asphyxia neonatorum is imputed to me which is widely different from that which I actually hold (Fundamentals of Asphyxia, *J. A. M. A.* **101**:261 [July 22] 1933). Even in the earlier paper quoted by Farber and Wilson, in which they represent me as stating that in asphyxia the respiratory "stimulus is not present" or "abnormally low," it was stated that the respiratory center is "depressed by asphyxia" (lack of oxygen) and that "more than the normal stimulus (of carbon dioxide) is required to induce breathing."

YANDELL HENDERSON, M.D., New Haven, Conn.

To the Editor:—We regret exceedingly that we have misstated Dr. Henderson's views, as he has noted. We should have used the expression "an adequate stimulus" (adequate amount of carbon dioxide) instead of "the normal stimulus."

SIDNEY FARBER, M.D., Boston.

Abstracts from Current Literature

Anatomy and Physiology

ROENTGEN EXAMINATION OF THE INFANT THORAX: A PRECISION TECHNIQUE. DAVID R. BOWEN, Am. J. Roentgenol. **27**:610 (April) 1932.

The author describes a restraining harness of flannelette with a sleevelike body which fits to a poplar board ¼ by 3 by 33 inches (0.64 by 7.6 by 83.82 cm.). The harness is so designed as to require no hand sewing other than basting, and by sewing machine only the simplest handicraft is needed. To the sleevelike body is fitted, first, a cap with drawstring. The first act of restraint is to tie this about the baby's head. Second, there are three short straps of the same material. Of these, the first two are brought forward and downward over the shoulders, while the third is drawn forward and upward over the perineum. Tapes, laced through loops in the free ends of these straps and through loops in a breast and body guard of single thickness, serve to hold the child firmly, save for the arms and legs. A 3 inch roller bandage 4 yards long, of the same flannelette, is run downward over the torso and legs—over the torso so lightly as to offer no restraint to breathing, and over the legs tightly enough to prevent kicking. The toes, left free, give an ever ready index of even the slightest discomfort. Finally, the arms are drawn forward, then upward and held extended beside the head. Wider straps, sewed to either edge of the sleevelike body immediately above the shoulders, are then drawn outward over each arm and tied at the back with a lower and a middle tape. The third, top, tape is passed backward and to the front, where it is tied over the hands. Grasping this tape gives the patient real comfort, and from this point, quiet sleep is routine. A slip block, 3 by 3 inches, with ¼ inch holes in the two free corners, is placed on the board above the cap in much the same way as index cards are held in place by adjustable back rests. Tapes, fastened to the upper border of the cap near the temporal areas, are passed through these holes and firmly tied. The head is thus drawn to the proper extension or chin lift, and rolling of the head is prevented. To induce crying, gentle closure of the nostrils generally suffices. The advantages of this apparatus are economy of film, comfort for the baby, simplicity (since all restraint may be applied in the nursery), saving of time and precision; i. e., all postures may be duplicated with a routine uniformity, of value for comparison not only with later studies of the same patient, but for research with groups of any number.

An all-aluminum frame of a top and base piece and parts for a cassette tunnel bracket are assembled on two lengths of brass pipe. Three legs, one at the top and two at the bottom, are incorporated, so that the frame can be used upright or horizontally. Holders for the poplar board are fitted to the top and base by slots and thumbscrews, so as to be universally movable in one plane. The board is received at the top by an adjustable tenon. A similar receptacle at the base can be opened and clamped shut by a thumbscrew. These fixtures allow 1 inch lateral adjustment, so that the child may be accurately centered even if its fixation to the board is off-center. A special casette tunnel of bakelite was found to be most useful for this apparatus.

STULIK, Chicago.

Pathology, Bacteriology and Biochemistry

THE PERMEABILITY OF THE RAT PLACENTA TO FAT. R. G. SINCLAIR, Am. J. Physiol. **103**:73 (Jan.) 1933.

Data are presented which show that the placenta of the rat, like that of the dog and of the rabbit, is permeable to fat.

NOURSE, Cleveland.

THE EFFECT OF EARLY GONADECTOMY ON THE GROSS BODY ACTIVITY OF RATS. C. P. RICHTER, Endocrinology **17**:445 (July-Aug.) 1933.

The effect of gonadectomy on the activity of eight male and seven female rats operated on from one to ten days after birth was tested by placing them in cages in which their running activity could be measured on revolving drums.

The activity of normal control animals increased until at one hundred and twenty days a plateau was reached at an average of about 10,000 revolutions daily, but with wide individual variations. The gonadectomized animals in fifty days reached a plateau of about 2,000 revolutions per day, with no individual differences.

The great consistency and the constant low level of the activity curves obtained from gonadectomized animals suggest their usefulness in testing various methods of replacement therapy.

JACOBSEN, Buffalo.

THE EFFECT OF MOLYBDENUM IMPURITY IN THE ARSENOPHOSPHOTUNGSTIC ACID REAGENT ON THE URIC ACID CONTENT OF BLOOD. V. I. KRIEGER, M. J. Australia **1**:677 (June 3) 1933.

If molybdenum-free sodium tungstate is used in the preparation of the arsenophosphotungstic acid reagent for the Benedict direct method of estimating uric acid, the method is capable of giving accurate results. If, however, molybdenum impurity is present in the reagent, grossly inaccurate values result, owing to the interaction with thionine and other substances in the protein-free filtrate.

GONCE, Madison, Wis.

MODIFICATION OF DEXTROSE BY INSULIN IN THE LIVING ANIMAL. J. THOMAS, Ann. de physiol. **8**:410, 1932.

The optical properties of dextrose isolated by dialysis from the blood of a normal subject demonstrated that this substance not only is made up of dextrose in stable equilibrium α and β but consists of a mixture of these sugars and another sugar with its characteristic optical property. The presence of the latter sugar seems to depend on the action of insulin in carbohydrate metabolism because in the blood of patients with severe diabetes not treated with insulin and in depancreatized animals only dextrose α and β, is found.

The blood of a diabetic patient was examined before treatment with insulin and three hours after insulin was injected. In the first sample only α and β dextrose were found; in the second α and β dextrose and another sugar having different optical qualities were found.

BUDSON, Ann Arbor, Mich.

CHANGES IN THE COMPOSITION OF THE BLOOD AND IN THE TONE OF THE VEGETATIVE NERVOUS SYSTEM OF COWS DURING PREGNANCY AND PARTURITION. L. SEEKLES, B. SJOLLEMA and F. C. VAN DER KAAY, Biochem. Ztschr. **249**:424, 1932.

In pregnant cows, until about four days before parturition there are no noteworthy alterations in the mineral composition of the serum. About this time, however, the calcium and inorganic phosphorus of the serum begin to diminish, and during parturition and shortly afterward the level of these constituents may rise or fall, indicating a lability of the mechanism for mineral regulation. The lowest values for calcium and phosphorus are obtained either just before or just after parturition, while the magnesium is increased at the same time. The serum potassium diminishes, reaching the lowest value a few days after parturition. The blood sugar increases during parturition. The acetone bodies also increase a few days before and after parturition, but during the latter they vary greatly. Generally a high content of acetone bodies coincides with a low sugar level, and vice versa. There are no changes in the nonprotein nitrogen of the blood. A

case of atypical paresis occurring at parturition has been observed in which the symptoms did not develop at the time the level of the serum calcium was lowest but when this had already risen considerably. The paresis could be overcome within ninety minutes by an intravenous injection of parathyroid extract, and although the total calcium level had actually diminished somewhat, the ionizable calcium fraction increased twofold. The disappearance of the muscular atony was attributed to the tonic effect of calcium ions on the muscles. It is not certain, though, whether this effect of the ions is direct or indirect. With the progress of gravity, a relative increase in the tonicity of the vagus of the heart seems to develop; this disappears again after birth. However, in only one instance was it possible to show that this increase in tonicity is accompanied by a rise in the phosphorus-calcium ratio, so that the hypervagotonia is the result of other factors as well.

KUGELMASS, New York.

ORTHODIAGRAPHIC EVALUATION OF THE SIZE OF THE HEART IN CHILDREN. OSKAR KIRSCH, Klin. Wchnschr. **9**:1574 (Aug. 23) 1930.

The author made an extensive study of the size of the heart in children by the orthodiagraphic method. He concludes that it is not permissible to use the relative width of the heart alone for diagnostic purposes. One should always correlate it with the length of the heart, and sometimes also with the sagittal diameter. The length of the body must also be considered in this connection.

STULIK, Chicago. [Am. J. Roentgenol.]

INVESTIGATIONS ON THE RESPIRATION OF CHILDREN. STEFAN FORMITTAG, Monatschr. f. Kinderh. **58**:249, 1933.

Investigations with a pneumograph showed the frequency of respiration in children to vary as shown in the following tabulation:

Age	Respirations per minute
1- 7 days	72-22
8-28 days	71-21
1- 6 months	58-21
½- 2 years	45-19
2- 5 years	40-21
5-10 years	31-15
10-15 years	31-14

The essential characteristic of the respiration of nurslings is its variability during light sleep; it frequently becomes irregular and reaches the higher figures. Deep sleep and sedatives, such as bromides, reduce the frequency.

The writer shows respiratory tracings characteristic of different types of respiration and demonstrates one curve which he believes hitherto undescribed. He believes that respiration is not controlled by one center but by several, just as various centers may assume responsibility for the action of the heart.

GERSTLEY, Chicago.

EFFECT OF IRRADIATED ERGOSTEROL ON PARATHYROID DYSFUNCTION. Y. KAWAKAMI and T. KURIBAYASHI, J. Pediat. (Tokyo), Aug. 20, 1933, no. 399, p. 1435.

The authors observed the effect of viosterol in parathyroidectomized animals. In cats the effect was marked, and the symptoms of dysfunction began to improve on the third day after administration of viosterol (from 0.2 to 0.5 cc. daily). It required from seven to fourteen days for the return of normal electric irritability. The blood calcium became normal, and the phosphorus also showed a slight increase with the administration of viosterol. Hypodermic and oral routes showed

no appreciable difference in effect on the animals. The toxic effect from an overdose of viosterol was shown by anorexia, emaciation, greatly lowered electric irritability and symptoms of hypercalcemia. A similar effect, though less marked, was obtained by daily irradiation with artificial sun rays.

In dogs, however, the improvement in symptoms was seen only when viosterol was combined with parathyroid extract-Collip. After the disappearance of symptoms, the parathyroid extract-Collip was withheld, and the animals continued to show improvement as long as the viosterol was given daily. The effect of overdosage was not as marked in dogs as in cats. In cats, parathyroid extract-Collip had no effect, as in dogs. The effectiveness of parathyroid extract-Collip in dogs, however, was of short duration (usually about twenty-four hours, when 25 mg. was given daily in two divided doses).

KATO, Chicago.

A METHOD OF ESTIMATING THE FUNCTIONAL ACTIVITY OF THE THYROID BY MEANS OF URINE OR SERUM: II. THE INFLUENCE OF THE ALKALINE EARTHS (CA, K, NA AND MG) ON THE FUNCTION OF THE THYROID. MUNLYONG KOH, Keijo J. Med. **4**:199 (June 30) 1933.

Two hours after the injection of an aqueous solution of calcium chloride into the vein of the ear of rabbits, there was a definite acceleration of the function of the thyroid. After a small dose of sodium chloride was injected, the functional activity of the thyroid was accelerated, but when a large dose was given, it was decreased. Both potassium chloride and magnesium chloride retarded the function. The author's method for determination of the function of the thyroid consists of adding 0.1 cc. of a 10 per cent solution of atropine sulphate to portions of urine and blood serum, which are incubated at 37 C. for two hours. Two drops of each preparation are applied to one eye of a cat, and the size of the pupil is measured from thirty minutes to four hours later. If the function of the thyroid is normal, 2 cc. of urine or 0.4 cc. of serum will be enough to inhibit the mydriasis caused by the atropine.

LEMASTER, Evanston, Ill.

A METHOD OF ESTIMATING THE FUNCTIONAL ACTIVITY OF THE THYROID BY MEANS OF URINE OR SERUM: III. THE INFLUENCE OF THE AUTONOMIC NERVES ON THE FUNCTION OF THYROID. MUNLYONG KOH, Keijo J. Med. **4**:222 (June 30) 1933.

The function of the thyroid gland of rabbits was accelerated by the injection of pilocarpine hydrochloride, but was decreased by injections of atropine and ergotamine. Increase in the function of the thyroid was produced by electric stimulation of the sympathetic and the vagus nerves for a short time and after nerves of either system had been severed. The function, however, was retarded by long continued stimulation and for an interval after the nerves were sectioned.

LEMASTER, Evanston, Ill.

CRITIQUE OF LANGER'S METHOD OF MEASURING THE ERYTHROCYTE SEDIMENTATION RATE: COMPARISON OF THE LANGER AND WESTERGREN METHODS. A. ELDAHL, Acta pædiat. **14**:356 (April 28) 1933.

If the pipet is allowed to stand in a slanting position, a variation of even 5 degrees from the perpendicular may increase the erythrocyte sedimentation rate by several millimeters in one hour. The author proposes an improved pipet stand to obviate this error. Comparative values, obtained in parallel determinations made on identical samples of blood, are given in the form of a graph which enables one to translate the data obtained by one of the two standard methods into the corresponding figures for the other method.

MCINTOSH, New York.

Nutrition

INTRADERMAL AND CUTANEOUS METHODS OF TESTING IN FOOD ALLERGY: A COMPARATIVE STUDY. JOSEPH T. BELGRADE, Arch. Dermat. & Syph. **27**:206 (Feb.) 1933.

The author reviews the literature concerning the work of many investigators in the study of reactions of the skin in food allergy, particularly the work of those who compare the use and results of the two methods of testing the skin—intradermal and cutaneous (or scratch).

Belgrade reports the results of a study of both methods used on fifty patients with conditions clinically diagnosed as allergy (eczema, urticaria, angioneurotic edema and erythema multiforme). Both methods with controls were used on each patient. The intradermal test gave 43.54 per cent positive reactions, while the cutaneous test gave only 15.45 per cent.

The author concludes that the intradermal test is more reliable and sensitive than the scratch test, and, if done carefully, is no more painful or dangerous (in regard to infection of the skin).

EKERMEYER, Iowa City.

STUDIES RELATIVE TO THE ESTIMATION OF VITAMIN D. LAWRENCE L. LACHAT, HENRY A. HALVARSON and LEROY S. PALMER, J. A. Off. Agric. Chem. **15**: 660, 1932.

Results produced by using thirteen rickets-producing rations on chickens are presented. (The technic of the method is described in detail.) One of the rations (yellow corn, 59; wheat flour middlings, 25; crude domestic casein, 12; precipitated calcium carbonate, 1; precipitated tribasic calcium phosphate, 1; dried baker's yeast, 1, and sodium chloride, 1), which gives an excellent rate of growth and produces uniformly low values for bone ash at 5 weeks of age, was used to obtain results (reported in detail) on the assays of vitamin D of twenty-two products, including eleven cod liver oils, four cod liver oil concentrates, two proprietary feeding supplements, one sardine oil, one burbot liver oil, one cod liver meal, one mineral feeding concentrate and one cod liver oil stearol. Considerable variation in the potency of vitamin D of the different substances was noted. A statistical analysis of the data concerning the time required for the assay showed that a period of four weeks of feeding with the method used was as accurate as a period of feeding of five weeks.

KUGELMASS, New York.

SIGNIFICANCE OF STUDIES OF KETOSIS AND OF NITROGEN AND WATER BALANCE TO OBESITY DIETS. J. I. ROWNTREE, J. Am. Dietet. A. **8**:307 (Nov.) 1932.

In advising rigid restrictions of food, the following factors must be considered: the effect of ketosis, the effect of a loss of nitrogen and the effect of an inadequacy of minerals or vitamins. Water balance and the relationship between the quality of food, the retention of water and the deviation of weight must also be considered.

That ketonuria is not incompatible with well-being was shown by McClellan and DuBois (1930). Ketosis does not result in the reduction of mental power. Wilder (1921) attributed the effect to anesthetic action, but concluded that ketosis has little effect on the nervous system. Depletion of the alkali reserve is the most undesirable effect of ketosis. Gamble, Ross and Tisdall (1923) showed that base is eliminated parallel to the loss of water rather than to the neutralization of acid. During a fifteen day fast, the elimination of base decreased to one fourth of that at first, while ketosis decreased one half. Weymuller and Ratner concur (1932) in these figures.

Wide variations in susceptibility occur. Deuel and Gulick (1932) found that ketosis appeared much sooner in women during fasting than in men, without relation to obesity. This, according to Greisheimer, is due to the smaller storage of glycogen in the liver in women.

That obese subjects are less subject to ketosis was shown by McClellan, Folin and Denis (1915), Deuel and Gulick (1932) and others. Obese subjects showed no

ketosis up to a ketogenic-antiketogenic ratio of 2.5, while normal persons did not exceed a ratio of 1.5 without ketonuria. Obesity does not predispose to ketonuria. Evans and Strang (1931) restricted obese subjects to 1 Gm. of protein and 0.6 Gm. of carbohydrate per kilogram of body weight; they remained in nitrogen balance without ketosis in spite of an intake of fat of from 200 to 300 Gm. Behre (1931) found the excretion highest in the afternoon, and lowest at night. McQuarrie (1929) and Deuel and Gulick (1932) demonstrated that fasting is more likely to result in acetonuria than a restricted diet of meat. Rony and Levy (1929) showed that fat and sugar tolerance and the rate of deposition are generally greater in obese persons.

McQuarrie (1929) found the requirements for protein markedly increased during dietary ketosis. Carbohydrate spares protein. With 0.33 Gm. of carbohydrate, 1.75 Gm. of protein per kilogram is adequate. With less carbohydrate, more protein is required. Folin and Denis (1915) found this less true of obese patients.

In determining the amount of nitrogen essential for equilibrium in dietary restrictions, Keeton, Mackenzie, Olson and Pickens (1931) found that fat spares protein as effectively as carbohydrate, if the diet is not too severely restricted. Gamble, Ross and Tisdall (1932) found a roughly constant ratio of protein to fat used for purposes of energy during a fast, the body protein being used proportionately to the amount of fat oxidized.

McQuarrie (1929) showed that less nitrogen was excreted on an alkaline ash than on an acid ash diet. Gamble, Ross and Tisdall showed that more calcium was excreted on an acid than on an alkaline ash diet.

Diets restricted in carbohydrate result in a sudden loss of weight out of proportion to the expenditure of energy. Pavy (1860) showed that 3 Gm. of water was held by 1 Gm. of glycogen in the tissues. Diets of fat produce a sudden loss of weight.

McClendon (1931) noted that an excessive intake of carbohydrate results in the retention of water in the body and an increase of blood volume. In dehydration, water comes from the muscles and skin. Folin, Trimble and Newman (1927) showed that dextrose is found temporarily stored in large amounts in the skin. Since the skin equals from 12 to 16 per cent of the body weight, it is important as a storehouse. The water content of the skin follows the amount of dextrose in the skin, being deposited and released with dextrose. McQuarrie (1929) believes that this is also influenced by the presence or absence of alkaline ash in the diet.

The author concludes as follows: 1. The most undesirable result of ketosis is an increased loss of nitrogen from the breaking down of protein for its ketolytic action. 2. Obese subjects are less susceptible to ketosis than subjects of normal weight. 3. Adequate base in the diet reduces loss of the nitrogen. 4. Acid balance favors the loss of water from the tissue.

PARKER, Rochester, N. Y.

INFANT FEEDING IN AN INSTITUTIONAL ENVIRONMENT. MAURICE L. BLATT and SAMUEL J. NICHAMIN, J. Pediat. **2**:469 (April) 1933.

At St. Vincent's Infant and Maternity Hospital, Chicago, powdered lactic acid milk has proved clinically more successful than any other milk products for the routine feeding of infants on a large scale. Whereas the mortality in the past was as high as 50 per cent at times, during the past decade the mortality has dropped to between 2 and 8 per cent. Infants under 8 months of age have shown an average gain of from 1½ to 2 pounds (from 700 to 900 Gm.) a month. The application of the newer principles of the nutrition of infants has given most satisfactory results.

LEMASTER, Evanston, Ill.

BACTERIA ON FRUIT. J. T. SMEALL, Brit. M. J. **2**:917 (Nov. 19) 1932.

A study of bacterial contamination of the surface of various fruits is presented. Experiments were conducted in order to show that washings contained fewer and fewer organisms. In most instances the organisms were of the nonpathogenic

group, but not infrequently the more virulent organisms were found. The suggestion is made that during the fruit-eating season gastro-intestinal disturbance may occur from excessive contamination of fruits by various organisms rather than from the fruit itself.

ROYSTER, University, Va.

THE RÔLE OF MINERALS AND VITAMINS IN GROWTH AND RESISTANCE TO INFECTION. ALAN BROWN and FREDERICK F. TISDALL, Brit. M. J. **1**:55 (Jan. 14) 1933.

This article includes: a general brief discussion of the minerals essential to the diet, and sections on the growth and resistance of animals; the part played by various vitamins, and an especially devised cereal which fulfils, according to the authors, the requirements for daily food. The article concludes with a caution to the effect that the content of vitamins and minerals in the food of the growing child should be watched more carefully

ROYSTER, University, Va.

VARIATIONS OF THE DEXTROSE AND OF THE SOLUBLE PHOSPHATES IN THE BLOOD OF THE NORMAL INFANT DURING DIGESTION. G. SANPAOLESI, Riv. di clin. pediat. **31**:135 (Feb.) 1933.

The author determined the blood sugar and blood phosphate curves of infants after the ingestion of food, which was either mother's milk or modified milk formulas. Nineteen composite curves are given for seventeen infants between 18 days and 6 months of age.

The blood sugar curves follow approximately those reported by other investigators. The blood phosphate curve shows a fall, reaching its minimum about an hour after the food is taken; this is essentially at the time when the blood sugar curve reaches its maximum. Each has returned to its normal value in from three to four hours.

The author feels that the blood sugar curve is largely controlled by a neurohormone reaction.

HIGGINS, Boston.

PERMEABILITY OF THE LARGE BOWEL TO FOREIGN PROTEIN IN INFANCY. EDWARD V. GYÖRGY and JULIUS SURANYI, Arch. f. Kinderh. **98**:151 (Jan. 24) 1933.

Intradermal tests with horse and cow serum gave positive results in infants after the serums had been administered as retention enemas. These results indicate that in infancy foreign proteins are absorbed unchanged through the large bowel.

LEMASTER, Evanston, Ill.

CALCIUM AND PHOSPHORUS METABOLISM IN RICKETS PRODUCED BY A DIET HIGH IN MAGNESIUM. GEORG MEYER ZU HORSTE, Monatschr. f. Kinderh. **57**:342, 1933.

In previous experiments the author showed that rickets could be produced in rats by a diet high in magnesium. His present investigations show that in the rickets due to magnesium the phosphorus balance and calcium balance diminish simultaneously. But in the rickets produced by the McCollum diet, no. 3413, the calcium balance does not diminish as rapidly as does the phosphorus, owing, presumably, to the high content of calcium in the diet.

In the recovery from rickets of either type the mineral balances are the same, though in one of the author's animals there was a decidedly better retention of calcium than of phosphorus.

Rominger, Meyer and Bomskov demonstrated that in the healing of infantile rickets the calcium balance does not improve until there has been a decided improvement in the retention of phosphorus.

The author concludes that infantile rickets and rickets produced experimentally in rats are not identical.

GERSTLEY, Chicago.

THE EFFECT OF SALT BATHS ON PROTEIN AND MINERAL METABOLISM. HUGO E. MEYER, Monatschr. f. Kinderh. **57**:355, 1933.

The effect of hot water and salt baths on metabolism was studied in six children aged from 3 to 10 years. In two of the children protein as well as mineral metabolism was studied. Hot water baths did not influence protein metabolism, whereas salt baths increased the excretion of nitrogen. Sulphur metabolism paralleled that of nitrogen.

The effect of the various baths on the phosphorus and the calcium metabolism was extremely variable.

Hot water and table salt baths had little effect on the relation of calcium to phosphorus, but brine baths benefited the calcium ratio.

GERSTLEY, Chicago.

THE DEPOT OF CHLORIDE. G. TOROK and A. KALLO, Monatschr. f. Kinderh. **57**:386, 1933.

In experimental work on growing and full-grown dogs, Torok and Kallo confirmed their previous work with infants; namely, the liver serves as a depot for sodium chloride. In this capacity the liver is much more active in the infant than in the adult. The experimental work of the authors consisted in the injection of solutions of sodium chloride into the portal veins and the analysis of the sodium chloride recovered in the hepatic veins and in the vena cava. There is much more retention of salt by the liver in the young animal than in the old. The infant, too, excretes much of the salt into the bile, although the content of the gallbladder is quite dilute.

Water metabolism is undoubtedly related to that of salt but is certainly not parallel.

The authors advance the theory that the amount of salt in the portal vein acts as a regulator of the amount excreted by the hepatic veins.

GERSTLEY, Chicago.

TOXICOSIS AND OTITIS MEDIA IN NURSLINGS. M. SALZBERGER and E. RABINOVICI, Monatschr. f. Ohrenh. **67**:188 (Feb.) 1933.

Salzberger and Rabinovici designate as toxicosis a nutritional disturbance occurring in infants in good health, usually in the first year of life. The condition is characterized by a sudden onset of vomiting and usually diarrhea, followed by apathy, loss of appetite and a rise in temperature. In severe cases the infants are stuporous or unconscious, the eyes are sunken, and the fontanels are depressed. The terminal stage is marked by tonic and clonic spasms and the appearance of coffee-ground vomitus. Toxicosis may have an alimentary, a parenteral or a mixed etiology. In Jerusalem it occurs mostly during periods of extreme heat and dryness. In eighty-two of the ninety-nine cases which form the basis of this report, otologic examination disclosed disease of the middle ear: in sixty-six cases, suppurative otitis media, and in sixteen cases, catarrhal or simple otitis media. Paracentesis was performed in all cases with positive results. Recovery occurred in thirty-seven cases and death in thirty-nine; in six cases the result was unknown. In a series of cases in which nutritional therapy was without result, including several grave cases in which interruption of feeding and injections of dextrose had proved useless, paracentesis produced a sudden improvement in the general condition. In twenty-seven of the cases in which there was no improvement despite a flow of pus from the ear, mastoidectomy was performed. In all but two cases the mastoid process was pathologically changed, and in most cases it contained pus, but this was not under pressure. None of these patients had exhibited any clinical symptoms of mastoiditis. Nineteen of the twenty-three patients operated on died; twenty-three of the fifty-five patients not operated on died. The authors do not think that otitis media and possible suppuration of the mastoid process caused the toxicosis. They think that the unfavor-

able climatic conditions of heat and dryness favored the occurrence of a disease appearing under two chief manifestations: toxicosis and otitis media. Satisfactory drainage of the pus in the ear may often exert a favorable influence on the course of the disease, but otologic therapy must be accompanied by nutritional and general therapy. Mastoidectomy should not be performed as a routine measure, but only in cases of otitis media in which paracentesis did not effect an improvement.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

ANTIRACHITIC VITAMIN OF RADICLES OF BARLEY. A. SCHITTENHELM and B. EISLER, Ztschr. f. d. ges. exper. Med. **75**:737, 1931.

During sprouting, the radicles of barley form an antirachitic substance without irradiation by rays of short wavelength. The direct test of the raw substance by its ability to heal rickets is not accurate because of the poor protective action. Extracts are suitable for test purposes and are capable of healing rickets. In prophylactic tests the raw substance was effective. Rats the diets (McCollum 3143) of which contained 6 per cent root substance remained healthy and showed good growth and normal composition of the bones.

In rickets the utilization of food by the rat is disturbed and the nitrogen balance is negative. Both growing and adult rats use radicles, especially if a dose of some antirachitic substance is given at the same time. The failure of the radicles to heal rickets in the rat is probably due to poor assimilation of food, a result of digestive disturbances.

Barley radicles sprouted in the complete absence of light contain an antirachitic substance which can be detected biologically. The substance is in the nonsaponifiable fraction of an acetone-methyl-alcohol-petroleum-ether extract and is isolated in the usual way. It may be identical with the active antirachitic material in viosterol.

KUGELMASS, New York.

THE FEEDING OF BUTTERMILK TO YOUNG BABIES FOR MANY WEEKS. B. E. J. H. BECKING, Maandschr. v. kindergeneesk. **2**:25 (Oct.) 1932.

After studying the clinical histories of a number of babies who were fed buttermilk from birth for many weeks, the author gained two impressions: As was mentioned by Marfan, there is a more or less critical period about the sixth or seventh week. When this critical time has passed, buttermilk may in many cases give a favorable result for many weeks.

VAN CREVELD, Amsterdam, The Netherlands.

THE RÔLE OF GLYCOGEN IN THE ORIGIN OF HYPERTROPHY OF ORGANS. S. VAN CREVELD, Maandschr. v. kindergeneesk. **2**:123 (Dec.) 1932.

In this extensive review some of the newer physiologic and pathologic conceptions of glycogen are reported. Then the rôle which glycogen, according to recent investigations, plays in the origin of hypertrophy of different organs is discussed. Hypertrophy of the liver caused by an accumulation of glycogen is especially mentioned. The changes in metabolism found by the author in two children with this condition are briefly communicated. Further, the newer findings as to hypertrophy of other organs caused by an accumulation of glycogen (idiopathic cardiac hypertrophy, renal hypertrophy, hypertrophy of the pyloric muscle) are discussed. The pediatric significance of the problem is stressed.

AUTHOR'S ABSTRACT.

BLOOD SUGAR AND ALKALI RESERVE IN CHILDREN WITH EXUDATIVE DIATHESIS. R. K. DYKHUIZEN, Maandschr. v. kindergeneesk. **2**:268 (March) 1933.

The author confirms the opinion of those investigators who believe that during the period of exudative diathesis, when the cutaneous symptoms are manifest, there

should exist a high blood sugar content and acidosis, both perhaps being related to sympathicotonia. Whether the sympathicotonia is the cause or the consequence of the eczema, he could not establish.

VAN CREVELD, Amsterdam, The Netherlands.

CONTINUED INVESTIGATIONS ON THE PROPHYLACTIC ACTION OF IRRADIATED ERGOSTEROL. J. J. SOER, Nederl. tijdschr. v. geneesk. **76**:4438 (Sept. 17) 1932.

The author examined the prophylactic influence of vitamin D given in the form of a Dutch preparation of irradiated ergosterol in rickets. To 224 children he gave during a long time a daily dose of 0.02 mg. With the exception of 3 who did not take the medicine regularly, all of the children remained free from rickets. This dose even seemed to be sufficient to cure manifest rickets, though somewhat slowly; but as a therapeutic dose the author recommends double the amount. In the second year of life rickets does not occur as frequently as is often assumed, but notwithstanding this it is advisable to administer prophylactic doses even then.

VAN CREVELD, Amsterdam, The Netherlands.

AN OBJECTIVE METHOD TO DETERMINE IN VIVO THE CALCIUM CONTENT OF THE BONES, ESPECIALLY IN RICKETS. J. J. DE DOES, E. GORTER and W. A. SEEDER, Nederl. tijdschr. v. geneesk. **77**:25 (Jan. 7) 1933.

A method of studying in vivo, objectively and quantitatively, the amount of calcium in the bones is described. The method is based on the standardization of the blackening of the photographic film for amounts of calcium per cubic centimeter by means of the microphotometer of Moll. By this method, which may also be applied in other diseases, it was found that during recovery from rickets there is not only an increase in the amount of calcium, but also a displacement of the concentration of calcium at the epiphyseal borderline.

VAN CREVELD, Amsterdam, The Netherlands.

Prenatal Conditions

CONGENITAL HEMIHYPERTROPHY: A REPORT OF EIGHT CASES. E. G. WAKEFIELD and EDGAR A. HINES, JR., Am. J. M. Sc. **185**:493 (April) 1933.

Eight cases of congenital hemihypertrophy are reported with tabulated summary, which brings the total number of cases reported in the literature to eighty. One of the eight cases was that of crossed hypertrophy. The ages of the patients ranged from 3 to 32 years; five cases were in males and three in females. The right side was hypertrophied in four patients, the left in three, and in one the hypertrophy was crossed. The mental status was normal in six cases; one patient was mentally deficient, and one was mute, of unknown mentality. No history of congenital familial anomalies was obtained. Four patients presented other congenital anomalies. Photographs from two of the cases accompany the article. The prognosis depends on the degree of hypertrophy and the age of the patient. The conclusion is that if there is no disability after normal growth is completed, there is no reason to expect it to occur.

HENSKE, Omaha.

DIAPHRAGMATIC HERNIA ASSOCIATED WITH SECONDARY ANEMIA. KENNETH D. GARDNER, Am. J. M. Sc. **185**:561 (April) 1933.

Twenty-eight cases (twenty-two previously published) are briefly summarized. Seventeen were in females and eleven in males. Nineteen cases occurred after the age of 40. Twenty-five were thought to be congenital, and three had a possible traumatic origin. Seven patients had no gastro-intestinal symptoms; nine had

gastro-intestinal symptoms for a period of months only. One had symptoms from childhood, and twelve had symptoms ranging from six to forty years in duration.

Of the twenty-eight cases, the diaphragmatic hernia was a primary factor in producing anemia in eight; true peptic ulcer complicated five other cases; insufficient data, postoperative death and the possibility of anemia of unknown origin eliminated three others, and the remaining twelve cases allowed only the supposition that the anemia was caused by the hernia. The anemia is secondary and is caused, it is assumed, by venous oozing due to compression of the stomach by the diaphragmatic muscles. The regimen consists in medical treatment for the ulcer and treatment for the secondary anemia. If these measures fail, surgical correction of the lesions should be considered.

HENSKE, Omaha.

POLYDACTYLIA. GEORGE GELLHORN, J. Missouri M. A. **30**:152 (April) 1933.

The author reports observation on an interesting family in which several members had polydactylia. The author points out that "genealogical studies in the literature and animal experimentation clearly indicate that polydactylia is an hereditary phenomenon the ultimate cause of which resides in the germ plasm. Polydactylia is often associated with physical deformities in other parts of the body and mental deficiency."

The reduplication of digits occurs most often on the outer side of the affected part, next on the inner side and rarely in the middle.

True polydactylia is produced by a split or fissuring of the bone, though a semblance of this is sometimes present, involving only the soft parts.

A new-born baby in the family reported on had six fingers on one hand and six toes on each foot. The mother's sister was born with six fingers and six toes, and in turn gave birth to two children each of whom showed the same anomaly on the hands and feet. In the rest of the family polydactylia was found in at least thirteen persons in six generations.

Close intermarriage has been shown to be a factor in this condition, and the occurrence of the anomaly apparently follows the mendelian law.

BERGER, Kansas City, Mo.

THE PREMATURE INFANT AS A PATIENT. T. COOK SMITH, H. S. ANDREWS and MARGARET LIMPER, South. M. J. **26**:293 (March) 1933.

The authors believe that the care of the premature infant begins at birth rather than a few hours after. Methods of resuscitation should be placed on a more scientific basis, and the responsibility for resuscitation should be assigned. All preparations should be made before the delivery.

There should be better methods of isolation. The attending personnel, both nurses and interns, should be changed as little as possible. If possible, premature infants should be treated by complete isolation.

SCHLUTZ, Chicago.

VITAMIN DEFICIENCY IN THE ANTENATAL PERIOD: ITS EFFECTS ON THE MOTHER AND THE INFANT. J. PRESTON MAXWELL, J. Obst. & Gynæc. Brit. Emp. **39**:764, 1932.

The author believes that vitamin deficiency may be more important during pregnancy than at any other period of a woman's life. It may make labor more hazardous and may affect the fetus in utero. Vitamins A, B, C, D and E are all important in this connection.

Vitamin A deficiency may interfere with ovulation; this vitamin is probably a prophylactic against puerperal infection and doubtless is stored by the fetus. Maxwell reports a case of congenital keratomalacia of both eyes in an infant born of a mother with osteomalacia. She was suffering from both vitamin D and vitamin A deficiency.

There is some evidence that vitamin B deficiency tends to produce abortion, and that it may be related, in an etiologic way, to postpartum hemorrhage and

hemorrhages of the newly born. Vitamin C deficiency in the mother may affect the fetus and give rise to antenatal deficiency and infantile scurvy. Maxwell mentions a case to illustrate this point.

Maxwell feels that he and others have proved that osteomalacia is a disease due to vitamin D deficiency, associated with lack of utilized calcium. The fetus is affected by this deficiency and is subject to fetal rickets. The author gives data on six cases. He believes these cases place fetal rickets as a distinct entity.

The effect of vitamin E deficiency has been demonstrated experimentally, and abnormal implantation and fetal resorption have been demonstrated. There is considerable doubt as to how far these data can be applied to woman in explanation of cases of apparent infertility.

Vitamins can be supplied if social and economic conditions are favorable and if the patient is cooperative. Further study is needed, and among other important problems, it may be possible to explain the etiology of hemorrhagic disease of the newly born, on the basis of vitamin deficiency.

ADAIR, Chicago.

A SMALL PREMATURE INFANT. J. D. HOULIHAN, Practitioner **130**:608 (May) 1933.

The author presents the case of a boy born prematurely at 6½ months, weighing 1 pound and 7½ ounces (666.22 Gm.) and 14 inches (35.48 cm.) in length. As a substitute for a hospital incubator, the baby was kept in a hot press in the bathroom at home. The temperature was maintained at from 90 to 95 F. The baby was fed on sugar-water and a formula of Nestlé's food. He gained from 2 to 8 ounces (57 to 227 Gm.) per week, and at the end of the twelfth week weighed 5 pounds and 10¼ ounces (2,558.54 Gm.).

SAPPINGTON, San Francisco.

SUPERNUMERARY MUSCLES OF THE MIDDLE EAR. F. ALTMANN, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **133**:28, 1932.

In microscopic serial examinations of a large number of malformed temporal bones, Altmann in three instances found supernumerary muscles in the middle ear. He describes the cases in detail because the finding of supernumerary muscles in the middle ear is rare, and because in one case the supernumerary muscles may have been of phylogenetic significance.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

RARE CONGENITAL CARDIAC ANOMALY. JOSEF SVEJCAR and ANNA FRANCOVA-HELBICH, Časop. lék. česk. **70**:1775 (Dec. 18) 1931.

The literature is reviewed. Congenital block is rare because embryonic and new-born tissues present none of the degenerative changes that usually produce block in later life. The case report gives the laboratory and cardiographic findings and in detail the observations at autopsy. The anatomic diagnosis was atresia of the pulmonary artery and of the region of the semilunar valves; persistence of the ductus arteriosus; patent foramen ovale; aortic dilatation; pulmonary hypostasis and bronchopneumonia; bilateral general venestasis; cyanosis, and general atrophy. The clinical diagnosis was atrophy; congenital heart disease; cyanosis of the newborn; bronchopneumonia; suppurative otitis media, and bilateral sino-auricular dissociation.

STULIK, Chicago.

A SINGULAR TYPE OF CHONDRODYSTROPHY. OTTO VYCHYTIL, Časop. lék. česk. **70**:1785 (Dec.) 1931.

The literature contains reports of four cases of this rare type of chondrodystrophy, also referred to as fetal hypoplastic chondrodystrophy or chondrodys-

trophia calcificans congenita. A review of the literature is followed by a discussion of the etiology, embryology and hypotheses. A complete case report is given of a premature infant weighing 2,250 Gm. lacking the classic facial expression; i. e., there was only a slight broadening of the root of the nose. Grossly there was a scoliosis; the arms and legs were relatively short, the left shorter than the right. The roentgenograms revealed the lack of centers of ossification, and in all the areas of cartilage there were many small, shotlike bodies (like foreign bodies). Detailed findings at autopsy and roentgenograms are presented. A bibliography is added.

STULIK, Chicago.

Diseases of the New-Born

ICTERUS NEONATORUM. CHARLES E. SNELLING, J. Pediat. **2**:399 (April) 1933.

The red blood count, hemoglobin and icteric index of twenty normal new-born infants were determined daily. Specimens of the stools of forty-two infants were collected during the same period for the determination of bile pigments. Sections of the liver of forty infants either stillborn or dying during the first two weeks of life were examined histologically. During the first three days of life there was little change in the levels of the erythrocytes and the hemoglobin, but following this period there was a gradual decline for two weeks. The icteric index averaged 47 at birth, rose rapidly to between 65 and 90 for five days, then dropped rapidly to 50, and gradually reached 16 by the thirteenth day. The excretion of bile pigments in the stool was at a minimum for the first three days of life, then rapidly rose concurrent with the fall in the icteric index observed in the blood. To relative hepatic insufficiency is attributed a very important rôle in the cause of icterus neonatorum. This temporary period of insufficient function may be due to the increased portal circulation after birth and to the discontinuance of hematopoietic activity in the liver. The histologic studies suggest that the endothelial cells of the liver do not assume the function of removing the bilirubin immediately at birth, but that, coincident with the change to the usual Kupffer cell, this function increases.

LEMASTER, Evanston, Ill.

MASSIVE COLLAPSE OF THE LUNG IN NEWBORN INFANTS. MURRAY H. BASS, J. Pediat. **2**:435 (April) 1933.

Three cases of massive collapse of the lung in new-born infants are reported. In each case the infants were acutely ill and were obviously suffering from respiratory difficulty. Physical examination showed dulness over the right lung, hyperresonance over the left lung, with vesicular breathing, and displacement of the heart to the right of the sternum. Bronchial obstruction is thought to be the most frequent cause of this condition.

LEMASTER, Evanston, Ill.

WINCKEL'S DISEASE. SILIK H. POLAYES and BENJAMIN KRAMER, J. Pediat. **2**: 482 (April) 1933.

A diagnosis of Winckel's disease was made in the case of an infant, aged 16 days, who showed jaundice, cyanosis, progressive anemia, a palpable spleen and liver, chocolate discoloration of the blood, methemoglobin and hematoporphyrin in the urine. Repeated transfusions of blood caused immediate improvement and eventual recovery.

LEMASTER, Evanston, Ill.

REPORT ON THE OCCURRENCE OF GONOCOCCIC VAGINITIS IN THE NEW-BORN. E. J. WYNKOOP and WINTHROP PENNOCK, New York State J. Med. **32**:1192 (Oct. 15) 1932.

Vaginal smears were taken from new-born infants on the first, fourth and thirteenth days of life. In all, 1,150 cases have been examined, and in none have

gram-negative intracellular diplococci been found. Nineteen, or 1.6 per cent of the cases, gave evidence of gonococcic ophthalmia. In 195 cases there were polymorphonuclear leukocytes in the smears on the first day, in 241 smears on the fourth day and in 494 on the thirteenth day. The presence of polymorphonuclear leukocytes in vaginal smears of the new-born is of little importance.

AIKMAN, Rochester, N. Y.

Acute Infections

THE TREATMENT OF COUGHS WITH SUPRARENAL: II. MEASLES. ORVILLE BARBOUR, Arch. Pediat. **49**:779 (Nov.) 1932.

Seventy-six patients with measles were treated with desiccated suprarenal gland. The author feels that a distinct amelioration of cough followed such treatment. No untoward results were obtained.

WADDELL, JR., University, Va.

ACUTE APPENDICITIS AS A COMPLICATION OF MEASLES. C. L. THENEBE, M. HIRSBERG and V. CENCI, Arch. Pediat. **50**:28 (Jan.) 1933.

The authors found few references concerning the incidence of acute appendicitis as a complication of measles. Several reports from the literature, however, are reviewed, and five cases of acute appendicitis complicating measles are reported in detail. It is thought that mechanical pressure on the blood vessels from the hyperplastic lymphoid tissue in the appendix and the ensuing of the usual secondary inflammation may be taken as sufficient logical reasoning on which to base the onset of acute appendicitis. The possibility of a relationship between streptococcic pharyngitis and appendicitis is suggested. Immediate operation is advised in all cases of acute appendicitis and measles as soon as a diagnosis is established.

WADDELL, JR., University, Va.

THE BLOOD PICTURE IN PERTUSSIS. H. E. THELANDER, H. G. HENDERSON and K. KILGARIFF, J. Pediat. **2**:288 (March) 1933.

Blood counts taken at frequent intervals during the course of active pertussis showed a constant and characteristic curve. For the first five to fifteen days there was no change in the lymphocytic count; then an abrupt rise began, and the number of lymphocytes rapidly increased for from eight to twelve days. A return to normal followed within the next twenty days. The highest lymphocytic counts were found regularly at the time the most severe attacks of coughing occurred. The polymorphonuclears were also increased in number during pertussis, but not nearly so much as the lymphocytes. It is suggested that extraordinarily high lymphocytic counts are due to extension of the pertussis bacilli into the small bronchioles, where the absorption of toxin is increased. When measles arose during the stage of active pertussis, leukopenia was found. In a case of pertussis in which scarlet fever and empyema developed, the lymphocytic curve was the same as that usually seen in pertussis, but the polymorphonuclear count rose and fell as secondary infectious processes appeared and subsided.

LEMASTER, Evanston, Ill.

B. DIPHTHERIAE, GRAVIS AND MITIS. H. J. PARISH, ELSIE E. WHATLEY and R. A. O'BRIEN, Brit. M. J. **2**:915 (Nov. 19) 1932.

This article includes a study to determine the validity of the two forms of diphtheria bacilli suggested, the gravis and the mitis. Various studies were made by the authors, including immunologic experiments, work on the response to antitoxin, tests of the virulence of the two forms and experiments on the potency of their toxin and on the severity of the infection in relation to the type. The original work done by Anderson and others in Leeds is discussed.

The article closes with the following paragraph: "The interesting association of the gravis bacillus with severe attacks of diphtheria found in the Leeds area is a local phenomenon. Since the implications of the term 'gravis' do not seem to have been substantiated by further inquiry, we would suggest that the name gravis be withdrawn in favour of some non-committal title such as 'starch-fermenting type.'"

ROYSTER, University, Va.

THE SERUM TREATMENT OF SCARLATINA AND ERYSIPELAS. HENRY BAXTER, Glasgow M. J. **118**:361, 1932.

The results of using scarlet fever streptococcus antitoxin prepared by two well known drug houses for scarlatina and erysipelas are given. The author found that the scarlet fever serum produced by one firm was efficacious in the treatment of scarlet fever, but not in that of erysipelas. In contrast, the scarlet fever serum produced by the other firm was efficacious in the treatment of erysipelas, but seemed to have no effect on scarlet fever. Those interested in knowing the manufacturers of the serums may do so by referring to the original article.

SNELLING, Toronto, Canada.

CUTANEOUS PASSIVE IMMUNIZATION AGAINST TETANUS. A. URBAIN, Ann. Inst. Pasteur **49**:103, 1932.

Favorable results were secured in the prevention and cure of tetanus intoxication or infection in guinea-pigs. Tetanus antitoxin, of a potency of 3,000 units (international) per ten cubic centimeters, was mixed with a petrolatum and hydrous wool fat base. The ointment, in lethal doses, was applied to the shaven and slightly scarified skin of test animals between twenty-four hours preceding the injection either of toxin or of spores mixed with staphylococci and three hours after such injections. This afforded a fair degree of protection; the action was specific.

MARSHALL, San Francisco. [ARCH. PATH.]

SKIN REACTIONS TO VARIOLA, VACCINIA AND VARICELLA. PAUL DURAND and ERNEST CONSEIL, Arch. Inst. Pasteur de Tunis **21**:73, 1932

Variola or vaccinia left a state of skin reactivity to either virus. This was not true of varicella; there was no reaction with varicella virus or with the heterologous viruses. The reaction is considered an immunity reaction distinct from the sensitivity group (tuberculin and others) and the "reactivity" group (diphtheria toxin, etc.). Varicella is thus considered as distinctly separate from related vaccinia and variola, and a means of checking relationships between animal pox diseases is afforded. The technic used consisted of intradermal inoculations of specially prepared antigen, following which local reactions were relatively rapid (in four or more hours). The phenomenon is thus not the usual immunity reaction to vaccine virus, the disadvantages of which are pointed out by the authors.

MARSHALL, San Francisco. [ARCH. PATH.]

TRANSFUSIONS OF BLOOD AND MALARIA. P. NOBÉCOURT, R. LIÈGE, GRODNITSKY and COMNINOS, Bull. Soc. de pediat. de Paris **30**:453 (July 12) 1932.

Two children acquired malaria through transfusions of blood from a donor who had malaria. The donor had never had any rigors, but he had traveled considerably in malarial districts, where he had taken quinine. His blood did not contain any parasites that could be demonstrated in slides, but the reaction of Henry (ferroflocculation and melanoflocculation), which is considered specific for malaria, was positive. The authors suggest that the blood of prospective donors who have been in countries where malaria is known to be endemic be tested for this reaction before their blood is used for transfusion.

BENJAMIN, Montreal, Canada.

FEEDING OF CHILDREN WITH TYPHOID FEVER. R. ANTONIO, Prat. pediat. **10**:533 (Dec.) 1932.

The author presents a rather academic argument for the more rational feeding of children with typhoid fever and related conditions. Instead of milk alone, he urges the use of well balanced diets with an adequate supply of minerals and vitamins.

DOOLEY, Kent, Conn.

MEASLES AND DIABETES: A CLINICAL HISTORY. MIGUEL ECHEGARAY, But. Soc. catalana de pediat. **2**:14 (Jan.-March) 1929.

At the onset of measles, when there was only a trace of sugar in the urine, the regular doses of 3 units of insulin twice a day were discontinued, with the result that the patient, a young boy, was in deep coma within twenty-four hours. He recovered after adequate treatment.

WATSON, Elmhurst, Ill.

ORIGIN OF SCARLATINA. V. DELFINO, Med. latina **5**:676 (Dec.) 1932.

At the recent French medical congress at Montpellier, Professors Sacquepée and Liégois, of Val de Grâce, described experiments with a serum prepared from a streptococcus obtained from a patient with mastoiditis unrelated to scarlet fever. They found that this serum had the same therapeutic effect as that of genuine anti-scarlatinal serum. They present arguments to show that the streptococcus is nonspecific, first, because no cultural characteristic allows its differentiation from other germs of the same type and, further, because its antitoxin, in spite of the fact that it is reproducible by injection of the streptococcus of scarlatina, does not affect complications.

VINTON, Brooklyn.

CLINICAL FEATURES OF THE MALARIA OF CHILDHOOD. R. JEMMA, Arch. f. Kinderh. **95**:227 (Feb.) 1932.

An excellent study of malaria in infancy and childhood is presented, which gives evidence of the author's wide experience and keen observation. It should be emphasized that regularly recurring chills and fever are rarely seen, nor is it common to find enlargement of the spleen in the acute forms. Diagnosis is difficult as the manifestations of malaria in childhood are extremely varied.

Under the acute form, the author discusses gastro-intestinal disturbances, changes in the nervous system, the urinary tract, the blood, the cardiovascular system, the respiratory system and the skin and the occurrence of edema. There may be loss of appetite, diarrhea and cylic attacks of pylorospasm. The meningitis may resemble that of tuberculosis or may be of the fulminating type seen in epidemic meningitis. Peripheral neuritis may be present. Attacks of hemoglobinuria are to be expected and may prove fatal. The hematopoietic system is more severely injured than in the adult and may lose its powers of regeneration. The heart beat is relatively slow in proportion to the temperature, and extrasystoles are frequent. There may be congestion of the lungs and asthma which do not yield to the ordinary treatment. The skin may show herpetiform or morbilliform eruptions. Circumscribed and transient edema is sometimes seen, or there may be more generalized edema developing with the rise in temperature.

Malaria may exist in a latent form, the acute manifestations being precipitated by some intercurrent infection or by a preventive inoculation. Among the complications, coincident tuberculosis offers a particularly unfavorable prognosis.

LESLIE, Chicago.

WHOOPING COUGH STUDIED WITH THE X-RAYS. CARL HUNERMANN, Monatschr. f. Kinderh. **57**:36 (Feb.) 1933.

In the catarrhal stage of whooping cough roentgenologic examination does not show much beyond the facts that the pulmonary fields are unusually clear,

the intercostal spaces seem wider and the ribs more horizontal than normal, and the diaphram may be somewhat lower than usual. More typical changes develop with the onset of the convulsive stage, about a week after the beginning of the typical paroxysms. Broadening of the hilar region is first noted, followed by the development of striations radiating first into the lower paravertebral fields and later into the upper ones. The striations may be so marked that they completely blot out the shadow of the heart. The picture is that of a triangle with its base on the diaphragm and its apex in the midline of the hilus. The author shows typical x-ray pictures. The triangle, first described by Gott, occurs in the severe cases, although it is present in about 40 per cent of the lighter attacks. It occurs more frequently in attacks of longer duration. Infection of the nose and throat seems to favor the development of the picture. Probably the pertussis virus predisposes to other infection; if coincidental nasopharyngitis is present, the combined perivascular, peribronchial and interstitial inflammations invariably produce the typical triangle. This triangle was seen before the clinical appearance of pneumonia in eighteen children in whom the disease later developed. The picture may be confused with the somewhat similar one which develops from bronchiolitis of influenza, tuberculosis or measles.

GERSTLEY, Chicago.

POLYNEURITIS AS A SEQUEL TO PARATYPHOID FEVER IN AN INFANT. CHARLES COHEN, Acta pædiat. **13**:53 (June 6) 1932.

In an infant, aged 14 months, paratyphoid B fever set in abruptly, with symptoms of digestive disturbance and meningeal irritation. As the general symptoms subsided, paralysis of the right circumflex and radial nerves persisted, causing the child to hold the arm in a peculiar attitude, with strong flexion of the elbow and thumb. The condition gradually disappeared in the course of three months.

McINTOSH, New York.

PERCUTANEOUS IMMUNIZATION AGAINST DIPHTHERIA. BUERGERS and F. VON BORMANN, Ztschr. f. Immunitätsforsch. u. exper. Therap. **76**:1, 1932.

In guinea-pigs given subcutaneous injections of anatoxin in quantities corresponding with those employed in man, a strong immunity developed. Toxin, anatoxin, extracts of diphtheria bacilli and vaccines rubbed into the skin did not lead to immunization, but it was produced by the rubbing in of proper quantities of anatoxin in the form of salves. There was a marked difference in the efficiency of various batches of salves. Infections of the mucous membranes (conjunctiva and vagina) did not effect local or general immunity in the animal, while subcutaneous injection produced a general as well as a local (mucosal) immunity. Buergers believes that it has not been proved that natural diphtheritic infection in man leads to immunity.

DAVIDSOHN, Chicago. [ARCH. PATH.]

TOXINS FORMED BY STREPTOCOCCUS ERYSIPELATIS. G. JACOBSOHN, Acta pædiat. **13**:244 (June 6) 1932.

The erysipelas strains of streptococci are relatively feeble producers of toxin. But if dosages are used which in reactive persons give a cutaneous reaction comparable to that produced by dilutions of toxins from scarlatinal streptococci, about half the subjects who give a positive reaction to the Dick test give a positive response to erysipelas toxin, while 11 per cent of those who gave a negative reaction to the Dick test react positively to erysipelas toxin. Antiscarlatinal serum readily neutralized large amounts of erysipelas toxin, while anti-erysipelas serum could not be shown to have any appreciable power for neutralizing Dick toxin. The author concludes that scarlatinal streptococci and streptococci from cases of erysipelas produce toxins that are related but not identical. These toxins are evidently complex substances.

McINTOSH, New York.

RECENT EXPERIENCE WITH POSTVACCINAL ENCEPHALITIS IN SWEDEN. C. KLING, Acta pædiat. **13**:274 (June 6) 1932.

Since 1929, postvaccinal encephalitis has been a reportable disease in Sweden. Its occurrence appears to be on the increase, the most recent figures giving a frequency of about fourteen cases per hundred thousand vaccinations, with a mortality of 14 per cent. The size of the vaccinal ulcer plays no part in determining the incidence of encephalitis. The period of incubation is from seven to twelve days, and in most instances the disease lasts from two to four days. Not infrequently other conditions producing symptoms of the nervous system (tuberculous meningitis, poliomyelitis) occur coincidently with vaccination and are wrongly reported as postvaccinal encephalitis.

McINTOSH, New York.

DELAYED TETANUS. S. LANGERT, Acta pædiat. **13**:300 (June 6) 1932.

A boy, 12½ years old, was admitted to the hospital for the treatment of osteomyelitis of the left femur. A week after admission he began to show signs of tetanus localized in the left hand and forearm. Two or three days later, with the appearance of generalized symptoms of tetanus, the correct diagnosis led to a closer search for a source in the left hand, and it was found that the boy had scratched his hand on a board about two weeks before admission (three weeks before the first tetanic signs). He recovered after a week of treatment with antitoxin.

McINTOSH, New York.

ENLARGEMENT OF THE SPLEEN IN VACCINIA. P. LEREBOULLET, Acta pædiat. **13**:318 (June 6) 1932.

The author calls attention to the fact that with a successful vaccination in an infant the spleen becomes enlarged and remains palpable for three or four weeks.

McINTOSH, New York.

SUCTION IN LARYNGEAL DIPHTHERIA. H. VON WILLEBRAND, Acta pædiat. **13**: 499 (June 6) 1932.

Following the example of Lynah, the author has applied suction in laryngeal diphtheria, using a curved metal cannula shaped something like an intubator and connected with a vacuum cleaner pump. His series of observations is small, comprising only ten cases, but it presents an encouraging decrease in mortality and in the number of cases of croup requiring intubation.

McINTOSH, New York.

Chronic Infections

TULAREMIA WITH SPECIAL REFERENCE TO THE SCHILLING DIFFERENTIAL BLOOD COUNTS. R. B. H. GRADWOHL, J. Missouri M. A. **30**:3 (March) 1933.

Three cases of the ulceroglandular type of tularemia were studied. The patients had marked clinical symptoms, and all showed agglutination to Bacterium tularense.

The blood picture in all cases showed leukocytosis, the count varying in case 1 from 8,550 to 17,050; in case 2 from 15,800 to 20,850 and in case 3 from 11,825 to 15,325.

The blood showed a typical shift to the left in all cases at all times during observation.

The patient in case 1 had neutrophilia, the number of cells varying from 66 to 89 per cent with a marked regenerative infectious blood picture. The patient in case 2 had a neutrophil count varying from 62 to 82 per cent, with an even more marked regenerative infectious blood picture. In case 3 there was a less severe neutrophilia, the count varying from 51 to 58 per cent with a less severe regenerative shift to the right.

Tables setting forth several blood pictures accompany the article.

BERGER, Kansas City, Mo.

SYPHILITIC INFANTILISM. A. G. MAITLAND-JONES, Proc. Roy. Soc. Med. **26:** 151 (Dec.) 1932.

The patient was 10½ years old. He weighed only 41 pounds (18.6 Kg.) and measured only 41 inches (102.5 cm.). He was the only living child; his mother had six stillbirths. His Wassermann test at the age of 8 years had been positive. All measurements were found to be infantile. He was mentally alert but backward for his age. Two lower central incisors were of Hutchinson type. The liver was large, and the lower edge was hard to the touch. There was a left internal strabismus. The eyegrounds were clear. Roentgenograms of the wrists and ankles showed no delay in ossification or evidence of bony disease. The sella turcica was normal.

WILLIAMSON, New Orleans.

CONGENITAL TUBERCULOSIS BY ASPIRATION OF AMNIOTIC FLUID. GEORGES GANDU, Ann. d'anat. path. **9:**891, 1932.

The author discusses the portals of entry of the tubercle bacillus in congenital tuberculosis, and reports a case in which the infection resulted from aspiration of infected amniotic fluid in utero.

MELNICK, Chicago. [ARCH. PATH.]

NODULAR ENLARGEMENT OF THE ARTICULATIONS OF THE FINGERS: ITS FREQUENCY IN CONGENITAL SYPHILIS. R. HISSARD, Ann. de dermat. et syph. **3:**806 (Sept.) 1932.

For two years Hissard has been finding a deformity of the fingers accompanying congenital syphilis with sufficient frequency to raise the question of its significance in that disease. Nineteen examples of articular dystrophy are recorded in the form of case reports; in twelve of the cases, congenital syphilis was proved; in six, it was probably present.

The deformity involves the joints of the fingers and occurs in two forms: the nodular form, which consists of an enlargement of the articulation such that an appearance of bunching or humping is imparted to the first phalanx, and the globular form. In some subjects, all the articulations are more or less deformed, save those of the thumb; in others, certain fingers may escape. In some cases, the fifth digit presents the anomaly known as the camptodactylia of Landouzy (permanent and irreducible inflexibility of the finger).

All these malformations are painless. Although normal movements are not impaired (except in camptodactylia), they appear to be awkward. Roentgenograms have revealed no bony deformity.

What is the pathogenesis of this disorder, and how should this group of deformities be classified? Should it be regarded as an attenuated form of the chronic, deforming rheumatism so often found in the young in congenital syphilis? The author does not think so for the following reason: The latter disease frequently begins with constitutional symptoms, the joints are painful, there is roentgenologic evidence of bony changes, and the rheumatism is polyarticular. The dystrophy of the fingers accompanying congenital syphilis, on the other hand, is characterized by insidiousness, indolence, absence of roentgenologic signs and mono-articular involvement.

Could the articular dystrophy be gononoccic in origin? Several of the author's patients have presented no evidence to support this view.

The possibility of fibrous rheumatism is suggested, but it would be difficult to accept this hypothesis without anatomic proof and in the absence of painful phenomena.

In two of the author's cases, large hands and feet and other acromegalic stigmas accompanied the deformities of the fingers. This suggests an endocrine factor, the exact influence of which will have to be determined by wider experience and further study.

If syphilis is to be considered as the etiologic factor, what is the mechanism in the production of these deformities? It is the author's opinion that syphilis acts indirectly through the intermediation of the endocrine glands. This is suggested by the inefficacy of antisyphilitic treatment in making any impression on the lesions.

The discussion is concluded with the statement that, although syphilis may not be the sole cause of this dystrophy, it is certainly the most frequent.

GANDY, Houston, Texas. [ARCH. DERMAT. & SYPH.]

INVESTIGATIONS IN TUBERCLE BACILLEMIA ACCORDING TO THE METHOD OF LÖWENSTEIN. ARVID WALLGREN, Arch. f. Kinderh. **95**:297 (Feb.) 1932.

At the International Congress of Pediatrics in 1930, Löwenstein reported a new method for isolating tubercle bacilli from the blood. Ten cubic centimeters of blood is taken in a special apparatus containing 1 cc. of sodium citrate solution and grown on a special medium with an egg-glycerin-asparagine base. He claimed to have obtained a high percentage of positive cultures even in conditions which are not generally considered to be tuberculous; for example, in twenty-two of twenty-seven cases of acute rheumatic fever, tubercle bacilli were isolated from the blood. The author collected blood from fourteen cases of erythema nodosum and from four cases of acute polyarthritis and sent the specimens to Löwenstein's laboratory for culture. Positive cultures were reported in twelve of the first group and in two of the second group, although in three of the cases the patients had failed to react to large doses of tuberculin.

LESLIE, Chicago.

SPIROCHAETA PALLIDA IN "DRY SMEARS." FELIX WEISS, Arch. f. Kinderh. **95**: 300 (Feb.) 1932.

The method described by Weiss for determining the presence of spirochetes consists in the following: A solution of brilliant cresyl blue is dried on a slide. The material to be studied (nasal secretion, conjunctival secretion or exudates from the skin or other sources) is placed on the slide and streaked across the dye in parallel strokes. After drying, a drop of cedar oil or Canada balsam is added and a cover slip placed in position. The preparation is studied with the oil immersion lens. The cells and spirochetes stand out as white bodies against a violet background. This method compares favorably with dark-field illumination in the identification of Spirochaeta pallida.

LESLIE, Chicago.

SEROLOGIC DIAGNOSIS OF TUBERCULOSIS BY THE BUFFER REACTION. KLINKE, Monatschr. f. Kinderh. **57**:49 (Feb.) 1933.

In previous investigations carried out in connection with Dr. Hensel the author showed that when old tuberculin is added to the serum of a person with active tuberculosis demonstrable changes in the buffer reaction of the serum can be quantitatively determined. In this communication he reports the results of an investigation of 489 cases by means of the buffer test, which he found quite reliable. The reaction is not as definite as the Wassermann reaction in syphilis, but Klinke found that it was positive in 94 per cent of the cases of active tuberculosis studied.

GERSTLEY, Chicago.

TUBERCULOSIS IN CHILDHOOD. H. KLEINSCHMIDT, Monatschr. f. Kinderh. **57**: 209, 1933.

The author states that one is so inclined to consider tuberculosis as resulting from inhalation that one overlooks many primary foci resulting from ingestion. He then gives brief reports of primary tuberculous infection of the gums, tonsils, ears and cervical lymph nodes. In the latter the extension was probably through the tonsils or the eustachian tube. In Lübeck recently, primary infections were reported in

the esophagus and in the stomach. In the unfortunate experience of that town, seventeen cases of meningitis were traced to a primary involvement of the abdominal lymphatic glands.

On the other hand, Kleinschmidt was not able to associate any clinical symptoms with calcified mesenteric lymph nodes.

He then discusses the arguments for and against the occurrence of congenital tuberculosis and cites several cases to prove its existence. He thinks that too much attention has been given to the postmortem observations and not enough to serologic tests. In his cases, the positive reactions occurring in the first three weeks certainly speak for congenital disease.

GERSTLEY, Chicago.

A CASE OF CONGENITAL TUBERCULOSIS. H. CHIARI, Virchows Arch. f. path. Anat. **285**:779, 1932.

Necropsy of an infant 13 weeks old confirmed the clinical diagnosis of general miliary tuberculosis and tuberculous meningitis. The tubercles, which were most numerous in the lungs, liver and spleen, were barely visible to the naked eye and were translucent. In the left lung was a partly calcified primary complex. In the liver were six partly calcified lesions, apparently as old as the primary focus in the lung. The lymph nodes at the hilus of the liver were caseous and partly calcified. The involvement of the liver and its nodes is also considered to have been a primary complex, as old as that of the lung. The author believes that infection occurred during the late intra-uterine period and led to primary involvement of the liver and the left lung.

SCHULTZ, Chicago. [ARCH. PATH.]

MILIARY TUBERCLES IN THE SKIN IN MILIARY TUBERCULOSIS. P. GEIPEL, Virchows Arch. f. path. Anat. **286**:591, 1932.

To three previously recorded cases of generalized miliary tuberculosis in which he found tubercles in the skin, the author adds two similar cases. The tubercles were situated either deeply or superficially in the corium; when they are superficial, the epidermis may also be involved. All the cases were in nurslings. Geipel has never seen tubercles in the skin in miliary tuberculosis in adults. The subcutaneous tissue, on the other hand, almost uniformly reveals the presence of tubercles in miliary tuberculosis at all age periods.

SCHULTZ, Chicago. [ARCH. PATH.]

A METHOD OF SEARCHING FOR TUBERCLE BACILLI IN THE GASTRIC CONTENTS. P. F. ARMAND-DELILLE, Acta pædiat. **13**:25 (June 6) 1932.

The technic, previously described elsewhere, is reviewed, and evidence of its practicability and popularity is cited.

MCINTOSH, New York.

TUBERCULOSIS OF THE CERVICAL LYMPH GLANDS SUBSEQUENT TO VACCINATION BY THE CALMETTE METHOD. C. E. BLOCH, Acta pædiat. **13**:40 (June 6) 1932.

A mother who was known to be tuberculous but in whom the process was considered clinically inactive gave birth to an infant weighing 3,500 Gm. The child was inoculated orally with B C G. The mother nursed the infant for five months, when it was boarded out. Some time before the fifth month the infant showed an occasional rise in temperature and the gradual development of a swelling on the side of the neck. The swelling increased, requiring incision when the child was 6½ months old. As drainage persisted in spite of treatment with ultraviolet irradiation, excision was undertaken at the age of 10 months. Histologic sections showed characteristic tuberculosis, but neither cultures nor inoculation of guinea-

pigs with material from the gland yielded tubercle bacilli. At this time the tuberculin test was faintly positive, and roentgen examination of the chest gave negative results.

Bloch argues that the inactive state of the mother's tuberculosis, the early age at which adenitis appeared in the infant, the faintness of the tuberculin reaction, the failure of the disease to spread, the negative cultures and the negative results of inoculation of guinea-pigs favor the interpretation that the organism responsible for the adenitis was B C G.

McIntosh, New York.

Actinomycosis of the Lung and Pleura in an Infant of Two Years. J. de Does, E. Gorter and G. Korthof, Acta pædiat. **13**:58 (June 6) 1932.

The authors give a brief report of a case of actinomycosis of the left lung with empyema and invasion of the thoracic parietes. Typical granules were found in the pus, and the organism was cultivated both aerobically and anaerobically. With the repeated aspiration of pus, the local application of tincture of iodine to the wall of the chest, the oral administration of 1 Gm. of potassium iodide a day and roentgen therapy, the patient improved considerably. The prognosis, however, remained grave. The period of observation covered less than two months.

McIntosh, New York.

Epituberculous Pulmonary Infiltration Following a Tuberculin Test. Theodor Frölich, Acta pædiat. **13**:90 (June 6) 1932.

The actual histology of so-called epituberculous infiltrations is admittedly unknown, but certain features argue in favor of its being composed largely of mobile elements — tissue fluid and lymphocytes or other wandering cells — rather than of fixed tissue cells or caseous material. Langer called attention to the fact that an epituberculous infiltration which has been observed to disappear spontaneously in the course of healing may be caused to reappear by the injection of as little as 0.1 mg. of tuberculin into the patient.

Frölich reports a similar case. A boy, aged 12 years, who was admitted to the hospital for the study of hematuria, gave positive reactions to the percutaneous and the Pirquet tests. The right pulmonary field showed a triangular shadow with its base resting on the hilus, which was interpreted as a tuberculous thickening of the interlobar pleura. After nearly two months of observation, during which the hematuria disappeared, the boy was given an intradermal injection of 0.1 mg. of tuberculin. There was a violent local reaction, with vesiculation and lymphangitis. The temperature rose to 38.9 C. (102 F.), and there were dyspnea and cough. A rapid and marked flare-up of the condition in the upper half of the right lung was demonstrable by the physical signs and by roentgenograms. Hematuria temporarily reappeared. Although the general symptoms improved sufficiently so that the patient could leave the hospital about five weeks after the injection of tuberculin, the pulmonary findings subsided much more slowly. Even after two years a compact hilar infiltration and an interlobar pleural line were visible in the roentgenogram.

McIntosh, New York.

Weight Curves of Infants of Tuberculous Mothers. I. Heineman and N. Malmberg, Acta pædiat. **13**:165 (June 6) 1932.

The question at issue is whether active tuberculosis in the mother is prejudicial to the health of the infant, provided the infant is removed from the mother immediately after birth and provided congenital tuberculosis is not present.

This study included forty infants of tuberculous mothers; all of the infants gave a negative reaction to tuberculin tests of the skin. The controls numbered eighty-three infants. The average period of observation for a single infant was a little less than five months. It was possible by using averages to construct weight curves for the entire first year, showing rates of gain of (1) infants exposed to tubercu-

losis whose weight at birth exceeded 2,500 Gm., (2) control infants of comparable weight at birth, (3) infants exposed to tuberculosis whose weight at birth was less than 2,500 Gm. and (4) nonexposed controls for group 3. No significant difference could be demonstrated between infants born of tuberculous mothers and those born of healthy mothers, even those with a low weight at birth in whom it has been traditional to regard the taint of the mother's illness as particularly affecting the vigor of the offspring.

The mortality figures for the group exposed to tuberculosis and for the nonexposed groups showed no significant difference, only, perhaps, that the infants of tuberculous mothers had a more favorable expectation of life.

In this study the feeding and general care of the infants in the test and control groups were strictly comparable.

McIntosh, New York.

Recovery from Miliary Tuberculosis in Childhood, with Residual Lesions in the Spleen. E. G. Hellgren, Acta pædiat. **13**:180 (June 6) 1932.

At the age of 3½ years the patient suffered from a febrile illness of some weeks' duration attended by abdominal pain, clouding of consciousness and signs of irritation of the central nervous system. Her reaction to the tuberculin test was positive at the time, and enlargement of the mediastinal nodes was demonstrable by roentgenograms. Later, after recovery from this attack, tuberculous osteoarthritis of the right knee developed, for which the patient entered the orthopedic service at the age of 7 years. Roentgen examination showed a calcified primary focus in the left lung, about 200 calcium shadows of miliary size in the spleen and similar foci in the liver and the mesenteric lymph nodes. These findings strengthen the inference that during the first stage of the illness there had been hematogenous dissemination of tubercle bacilli.

McIntosh, New York.

Internal Diseases

Transient Pachymenia of the Intima of the Aorta with Reference to Juvenile Arteriosclerosis. C. Magarinos Torres, Am. J. Path. **8**:455 (July) 1932.

The thickness of the intima of the aorta in a group of twenty children between the ages of 2 days and 10 years showed a marked variation, attaining a maximum of 100 microns in the posterior portion. These local areas of increased thickness are due to the presence of a thick, cellular subendothelial layer. This chain is not related to age or to degenerative and nonspecific inflammatory processes, but must be considered as a transient physiologic change which disappears. It is probably due to a difference in the rate of growth of two adjoining portions of the aorta. In addition to this type of lesion, the author observed fatty changes about the mouths of the intercostal arteries.

Moore, Charlotte, N. C.

Multiple Manifestations of Subchondral Necrosis (Osteochondropathia Juvenilis, Osteochondritis and Epiphysitis). W. C. Martin and Hugo Roesler, Am. J. Roentgenol. **26**:861 (Dec.) 1931.

There is in the literature an increasing number of disease entities affecting the skeleton of young and growing persons. They are clinically benign and show a tendency to heal. Roentgenologically, the lesions, although in various bones, show great similarity. These diseases, described by Calve, Legg and Perthes, Osgood and Schlatter, Kohler, Keinbock, Preiser and others, have had rare localizations, as in the patella, condyles of the femur, apophysis of the calcaneous, astragalus, sesamoid bones, clavicle, capitulum and caput humeri, the heads of the metacarpal and the metatarsal bones. The reported case has a multiplicity of foci limited to the subchondral bone, and as most of these lesions have been described as separate entities, it is possible that these cases are all of the same

disease, with limitation of the lesion. In this case lesions were found in the spine, wrists, ankles, sesamoid bones, elbows, hips, ribs and metatarsal bones. Symptoms began at 11, and in early adult life there was an ankylosed left hip without other gross defect.

STULIK, Chicago.

SPLENECTOMY IN PURPURA HEMORRHAGICA. ELDRIDGE L. ELIASON and L. K. FERGUSON, Ann. Surg. **96**:801 (Nov.) 1932.

A review of the literature points to the fact that purpura haemorrhagica is a disease causing not only a reduction of blood platelets but a disturbance of the entire reticulo-endothelial system. It has not yet been proved that the spleen is the organ at fault in purpura haemorrhagica, but splenectomy appears to be the most effective method of controlling extensive hemorrhage of either the acute or the recurring type. Authorities agree that the results are more satisfactory in children than in adults, and the prognosis is better the earlier in the disease splenectomy is done.

Five new cases of purpura in which splenectomy was done are reported, and 108 cases from the literature are reviewed.

BANTIN, Omaha.

AGGLUTINATION REACTIONS IN RHEUMATOID ARTHRITIS: I. AGGLUTINATION REACTIONS WITH STREPTOCOCCUS HEMOLYTICUS. M. H. DAWSON, M. OLMSTEAD and R. H. BOOTS, J. Immunol. **23**:187 (Sept.) 1932.

The authors studied the serums of a large group of patients with rheumatoid arthritis for the presence of agglutinins for hemolytic streptococci. As a control, serums from a large group of patients with other diseases and from normal persons were used. For agglutination antigens several "typical strains" of Cecil, Nicholls and Stainsby, hemolytic streptococci from various other sources and various strains of other gram-positive cocci were used.

They found that a high percentage of the serums from patients with rheumatoid arthritis agglutinated hemolytic streptococci to very high titers. No correlation was obtained between the source of the strains and their agglutinability. Strains isolated from scarlet fever and erysipelas were agglutinated to as high a titer as the "typical strains" of Cecil, Nicholls and Stainsby. With few exceptions, control serums did not agglutinate the various strains of hemolytic streptococci. Other gram-positive cocci were either not agglutinated or agglutinated to a very low titer. There was one exception to this in the case of the "rough" pneumococcus, which was agglutinated to almost as high a titer as the hemolytic streptococci.

FOTHERGILL, Boston.

PNEUMONIA IN CHILDREN. MAUD L. MENTEN, SADIE F. BAILEY and FRANCES M. DEBONE, J. Infect. Dis. **51**:254 (Sept.-Oct.) 1932.

The authors studied from a bacteriologic standpoint the lungs of 131 children who had died of pneumonia and found: (1) Streptococcus viridans in 50 per cent; (2) Streptococcus haemolyticus in 23.7 per cent; (3) both of these types in 6.9 per cent, and (4) pneumonococcus (81.6 of type IV) in 45.8 per cent. The pneumococcus invariably occurred with other organisms.

TOOMEY, Cleveland.

THE HEMOLYTIC HEMOPHILIC BACILLUS ("BACILLUS X") IN SUBACUTE BACTERIAL ENDOCARDITIS. LEROY D. FOTHERGILL, MARIAN SWEET and JOHN HUBBARD, J. Pediat. **1**:692 (Dec.) 1932.

This is the second reported case of fatal subacute bacterial endocarditis due to the hemolytic hemophilic bacillus. The bacteriologic characteristics of the organism are described, as well as the clinical course of the disease.

LEMASTER, Evanston, Ill.

INFECTIOUS (SUBACUTE BACTERIAL) ENDOCARDITIS WITH CEREBRAL THROMBOSIS. M. G. PETERMAN, J. Pediat. **1**:699 (Dec.) 1932.

Subacute bacterial endocarditis with cerebral thrombosis occurred in a 7 year old girl. For three and a half months before she became acutely ill, she had frequent bleeding of the nose. Blood cultures made during life showed Streptococcus viridans. The clinical course during three and a half months in the hospital is described. Autopsy showed the usual changes of subacute bacterial endocarditis with thrombosis and softening in the left rolandic area of the brain, which had caused right hemiplegia.

LEMASTER, Evanston, Ill.

INFLUENCE OF THE AGE FACTOR ON THE FREQUENCY AND MONTHLY SEASONAL INCIDENCE OF RESPIRATORY INFECTIONS. C. C. MCLEAN, J. Pediat. **1**:729 (Dec.) 1932.

During a period of ten calendar years in which 156 children were observed for an exact period of four years from the date of their birth, 1,255 respiratory infections were seen. The patients were placed in two groups of 78 patients each, and the number of respiratory infections seen in the two groups during the first, second, third and fourth years of life, when analyzed, showed evidence that the age of the child influenced both the number and monthly seasonal incidence of the infections. In 28 of the 156 children during an epidemic year of respiratory infections, the monthly seasonal incidence was influenced more by the age of the child than by the epidemic.

LEMASTER, Evanston, Ill.

ARGYRIA: REPORT OF A CASE IN A PATIENT AGED FIVE AND A HALF YEARS. LAWRENCE T. ROYSTER, J. Pediat. **1**:736 (Dec.) 1932.

Argyria developed as a result of repeated irrigations of the nose with neosilvol solution. A functional heart murmur along with blueness of the skin had led previously to an erroneous diagnosis of heart trouble. Sections obtained by biopsy showed brown pigment in and around the basal layer of the sweat glands.

LEMASTER, Evanston, Ill.

VON RECKLINGHAUSEN'S DISEASE IN CHILDREN: REPORT OF A CASE PRESENTING PIGMENTATION AND BONE CHANGES. SIDNEY D. LEADER and MILTON J. H. GRAND, J. Pediat. **1**:754 (Dec.) 1932.

A case of von Recklinghausen's disease in an 11 year old American boy is reported. Brown patches had been present on the skin since birth. The bones appeared normal in the roentgenograms, except for a region of decreased density on the medial aspect of the distal end of the left femur. There were no subcutaneous nodules. Intelligence was unimpaired. No family history of the disease could be elicited. Similar cases of von Recklinghausen's disease reported in the literature are discussed.

LEMASTER, Evanston, Ill.

DISORDERS OF INTERNAL GLAND SECRETION IN CHILDREN. FRITZ B. TALBOT, J. Pediat. **1**:766 (Dec.) 1932.

This is a critical review of the fundamental proved facts concerning the normal and abnormal functioning of the various endocrine glands, with special attention to their rôle during childhood. The physiology of each endocrine gland is discussed separately, and the chief characteristics of its various dysfunctions are briefly cited, including remarks on laboratory findings and therapy. Talbot states that although there is considerable proof of interrelation between the endocrine glands, the data are so conflicting that it is more rational at present to approach the problem from the point of view of the individual gland, rather than to confuse the picture with double or multiple diagnoses.

LEMASTER, Evanston, Ill.

PRIMARY CHRONIC SPLENOMEGALY (BANTI'S DISEASE). B. M. FRIED, New England J. Med. **207**:595 (Oct. 6) 1932.

There is one group of splenomegalies still regarded as primary, in which an early removal of the spleen results, in many instances, in cure. This group, of which Banti's disease is an example, belongs to the sclerogenic disorders.

Fried reports the case of a boy, aged 10, with a history of profuse gastric hemorrhages of six years' duration. The results of the Wassermann and Kahn tests were negative. The erythrocyte count totaled 1,720,000 per cubic millimeter; the white cells, 10,600 per cubic millimeter; the platelets, between 120,000 and 140,000 per cubic millimeter, and the reticulocytes, 26 per cent; the hemoglobin was 40 per cent. There were moderate anisocytosis and poikilocytosis; also a slight diffuse polychromatophilia. The icteric index was 9.6. The bleeding and clotting time and the result of the fragility test were within normal limits. The blood culture and the results of the Widal test and the Pirquet tuberculin test were negative. The stools showed the presence of occult blood with the benzidine reagent. Roentgen examination showed no abnormalities in the lungs; the heart was enlarged. In the bones there was slight atrophy of the left tibia and also of the muscles of the lower part of the left leg, due to what was probably poliomyelitis at 1½ years. The patient was not operated on.

At necropsy, the spleen showed diffuse fibrosis of about two thirds of the organ. The sinuses were narrow and bloodless, their lining cells showing swelling and proliferation, and their lumens containing free macrophages. The follicles, too, showed fibrosis. The liver and the other abdominal viscera were not remarkable except for the lesser omentum, which showed fibrosis.

GENGENBACH, Denver.

LYMPHOSARCOMA. MAY OWEN, South. M. J. **25**:1248 (Dec.) 1932.

This condition occurred in a boy aged 3 years. His disorder began with a complaint of sore throat and weakness. A diagnosis of diphtheria was first made, and antitoxin was given in liberal quantities.

After hospitalization, a diagnosis of agranulocytosis was made on the basis of a low leukocyte count, marked decrease in granulocytes and foul necrotic membrane covering one tonsil. There was a general increase of all the lymph nodes. This continued after the condition in the throat showed improvement.

A mediastinal tumor was found. After about the third month from the onset of the disease, the leukocyte count varied from 800 to 13,800 per cubic millimeter with a neutrophil count of from 3 to 59 per cent, and a lymphocyte count as high as 96 per cent.

The case terminated fatally. No form of treatment gave any relief from symptoms.

SCHLUTZ, Chicago.

APHONIA AND CONGENITAL HEART DISEASE. REGINALD LIGHTWOOD, Proc. Roy. Soc. Med. **25**:1227 (June) 1932.

The case reported occurred in a baby 4½ months of age. She had been able to cry for the first five weeks; then suddenly she could make no noise on crying. She suffered from congenital disease of the heart. Recurrent involvement of the left laryngeal nerve has been described in cases of patent ductus arteriosus, and a dilated left auricle also might exert pressure on this nerve. However, in this case, when laryngoscopic examination was made the cords could be seen to abduct freely, though somewhat imperfectly, and such findings are not characteristic of organic recurrent involvement of the laryngeal nerve.

WILLIAMSON, New Orleans.

RENAL DWARFISM. A. G. MAITLAND-JONES, Proc. Roy. Soc. Med. **25**:1228 (June) 1932.

This case was reported in a boy of 4 years. The past history, the results of physical examination, roentgenologic report and urinalysis and the results of examination of the blood are given fully in the report.

WILLIAMSON, New Orleans.

LIPODYSTROPHIA PROGRESSIVA. A. G. MAITLAND-JONES, Proc. Roy. Soc. Med. **25**:1232 (June) 1932.

A case of lipodystrophia progressiva was reported in a boy of 11 years.

WILLIAMSON, New Orleans.

A CLINICAL AND PATHOLOGICAL STUDY OF BRONCHIECTASIS. H. H. MOLL, Quart. J. Med. **1**:457 (July) 1932.

The author's observations in a study of fifty-five autopsies and thirty-seven clinical cases are presented, along with a discussion of the various types and pathogenesis. He points out that bronchiectasis is primarily a disease of the young, 50 per cent of his patients having the onset during the first five years of life. The highest mortality occurred during the first five years of life, and nearly two thirds of the patients died before reaching the fourth decade.

Excellent plates showing the various types of the disease are appended.

BRADFORD, Rochester, N. Y.

INTESTINAL POLYPOSIS. RAOUL BENSAUDE, PIERRE HILLEMAND and PIERRE AUGIER, Arch. d. mal. de l'app. digestif **22**:473 (May) 1932.

Described as early as 1725, essential intestinal polyposis is a rare condition, being found only five times in a series of seventeen thousand autopsies. About one hundred and fifty cases have been described. The authors add eleven more cases to the literature. They emphasize the familial relationship of the disease, and note that it occurs most frequently between the ages 10 to 20 and 30 to 40. Diarrhea and hemorrhage are the fundamental and constant symptoms. The condition is rarely recognized without proctoscopy.

The authors discuss the proper method of obtaining good roentgenograms, the association of infantilism with this condition and the changes in the distal phalanges of the fingers which are characteristic when present.

Polyposes associated with intestinal parasites and inflammatory polyposis of undetermined origin are discussed. The pathologic anatomy and pathogenesis receive adequate attention, and a detailed explanation of the treatment is given. The article is illustrated with many photographs and roentgenograms. It is well documented with more than two hundred references to the literature.

ARTHUR R. TURNER, Chicago.

TWO NEW CLINICAL SIGNS OF AURICULAR TACHYCARDIA (AURICULAR FLUTTER). C. LAUBRY, DANIEL ROUTIER and A. VAN BOGAERT, Arch. d. mal. du cœur **25**:321 (June) 1932.

The authors describe their two new clinical signs of auricular flutter as being: (1) inequality of the pulse and (2) the appearance in diastole of a third sound, giving rise to a triple rhythm, characterized by continued variability; that is, the third sound does not occupy a fixed place in diastole. Electrocardiograms from the three cases studied are reproduced in the text.

ARTHUR R. TURNER, Chicago.

URINARY LITHIASIS IN CHILDREN. S. MEKLER, Arch. de méd. d. enf. **35**:652 (Nov.) 1932.

Writing from Palestine, Mekler declares that urinary calculi are much more common among children in that country than in European districts. As with adults, in whom lithiasis is extremely common, oxalic acid calculi are usually encountered. Of fourteen cases in Jewish children, twelve were instances of oxalic acid stone and two of uric acid. Nine of these children were boys, and five were girls. In at least half of the patients there was a hereditary predisposition. Instead of belonging to the leisure class, most of the patients come from the poorer strata, with no history of excessive consumption of nitrogenous food.

AMESSE, Denver.

EFFICACY OF INTRAVENOUS INJECTION OF SODIUM SALICYLATE IN A CASE OF STILL'S DISEASE. L. LEMIERRE and D. MAHONDEAU-CAMPOYER, Gaz. d. hôp. **105**:1029 (July 9) 1932.

The author reports the case of a patient who could not walk or use her hands for more than a year. While sodium salicylate given by mouth in large doses was ineffective, pain disappeared and free motion of the joints promptly returned after ten daily intravenous injections of the drug in 10 per cent solution of dextrose in doses increasing from 0.5 to 4.5 Gm.

Improvement continued during the ten months of observation.

KAJDI, Baltimore.

PATHOGENESIS AND THERAPY OF ASTHMA. M. GAUCHER and M. ALBEAUX-FERNET, Gaz. d. hôp. **105**:1093 (July 23) 1932.

This report is chiefly a review of the French literature. The actual asthmatic attack presupposes three conditions: (1) local lesions — disturbances in the respiratory tract (tuberculosis, chronic bronchitis, sclerosis, etc.), nasopharyngeal conditions, digestive disturbances (in children, hypochlorhydria in more than half of the cases); (2) constitutional factors, such as heredity, labile equilibrium of the vagosympathetic system and endocrine disturbances; (3) provoking agents — in most cases of an anaphylactic nature, in some cases colloid lability without any specific hypersensibility (attacks provoked by physical exertion and barometric and temperature changes), and sometimes direct irritation, such as inhalation of powders, or gases. For the treatment of the actual attacks ephedrine is recommended, and in severe cases, epinephrine. Etiologic treatment consists in desensitization, treatment of any focus, modification of the vegetative innervation and roentgen therapy of the spleen or the mediastinum.

KAJDI, Baltimore.

A CLINICAL STUDY OF CASES OF ANEMIA OF OBSCURE ORIGIN. C. DE LANGE, Rev. franç. de pédiat. **8**:448, 1932.

Six cases of anemia are reported. The first four give an impression of an infection of unknown origin. The fifth offers no explanation, and the last was probably due to a congenital debility. The author calls attention to the fact that in lymphatic leukemia the red cells are frequently destroyed, and that in an aleukemic interval, such a picture of anemia might be found.

SANFORD, Chicago.

FATAL ULCERATIVE ESOPHAGITIS IN THE COURSE OF ACUTE GASTRO-ENTERITIS. A. COSTA and A. FIANO, Scritti med. dedicati a Carlo Comba, ediz. Riv. di clin. pediat., 1929, p. 719.

The author reports the cases of two infants, one 7 months old and breast fed, and the other 50 days old and bottle fed, who died of hemorrhages from ulcers of the esophagus. The children had had acute diarrhea and vomiting preceding the hemorrhages, and were distinctly athreptic.

The occurrence of ulcers of the esophagus in children with gastro-enteritis of a toxic and infectious type is rare; the presence of blood in the vomitus should make one suspect such a condition.

HIGGINS, Boston.

ESOPHAGEAL ULCER WITH PYLORIC SYNDROME AND HYPOPLASTIC ANEMIA IN A CHILD OF TWO YEARS. M. ACUÑA, M. T. VALLINO and F. DE FILIPPI, Arch. argent. de pediat. **3**:418 (July) 1932.

Early symptoms were persistent vomiting, pain in the epigastrium, pallor and progressive loss of weight. Occult blood was observed in the stool.

Hygienic and dietetic treatment and the use of maternal blood did not improve the patient's condition. Ulcer of the stomach or of the duodenum was suspected, but was not found at the time of operation.

Autopsy showed a patent pylorus and absence of gastro-intestinal lesions, but an ulcer was found on the anterior wall of the lower third of the esophagus. The ulcer appeared to be a primary lesion of undetermined cause. There was no syphilis or tuberculosis and no particular pathologic alteration of the vessels. The condition is extremely rare, and the authors believe this to be the first case reported.

The usual forms of gastro-intestinal roentgen examination did not reveal the disorder. The symptoms resembling pyloric obstruction were probably due to a reflex effect from the ulcer. The progressive anemia was doubtless due to the persistent concealed bleeding from the area of the ulcer.

SCHLUTZ, Chicago.

SEDIMENTATION RATE. MIGUEL A. JAUREGUY, Arch. argent. de pediat. **3**:541 (Sept.) 1932.

The author reports sedimentation rates for pneumonia, rheumatism, diphtheria and tuberculosis.

In pneumonia, the rate declines with the development of the crisis. Sometimes this decline is interrupted coincident with a precritical period. The author believes that such a rise in the sedimentation rate indicates a temporary decline of immunity.

In rheumatism, the rate drops with improvement in the condition.

The sedimentation rate seems to be independent of and uninfluenced by cardiac lesions. Salicylic acid poisoning raises the rate.

In diphtheria, the rate is increased during the period of severe angina, indicating a diminution of immunity during this period.

It is not possible to predict the malignancy of the angina or its probable course by the behavior of the sedimentation rate.

The appearance of urticaria raises the rate.

In tuberculosis, the rate is raised if immunity to the disease is low; it falls with improvement in the condition and has no particular diagnostic significance.

SCHLUTZ, Chicago.

NECESSARY FUNCTIONAL TESTS OF THE KIDNEYS IN PEDIATRICS. P. P. NOGUEIRA, Arch. de med. infant. **1**:84 (Feb.) 1932.

In cases of renal disease the author employs the following functional tests: dilution and concentration test of Volhard, urea and creatinine test, indigo carmine test, chemical analysis of the blood and proteins of the serum, the constant of Ambard, the congo red test and the modification of the Volhard test by the injection of solution of pituitary.

SANFORD, Chicago.

SUDDEN DEATH IN CHILDHOOD. W. PIAGGIO GARZON, Arch. de pediat. d. Uruguay **3**:332 (Aug.) 1932.

Sudden death is most frequently observed during the first year of life. It occurs much less frequently in the older child than in the adult.

The infant is much more reactive than the older child or the adult. He is hyperemotional and hypersensitive. In his neurovegetative system the pneumogastric nerve predominates. A hypervagotonic state is almost physiologic for the infant.

The equilibrium of this state is easily disturbed.

The author does not believe that much importance attaches to the thymus or to pathologic conditions of the thymus in sudden death of the infant. He believes that practically all cases of sudden death are due to extrathymic causes. Cardiovascular lesions are rarely the cause of sudden death in the infant or the older child.

SCHLUTZ, Chicago.

REPORT OF A CASE OF LYMPHOGRANULOMATOSIS. F. NICOLA REYES, Arch. de pediat. d. Uruguay **3**:343 (Aug.) 1932.

Lymphogranulomatosis occurred in a child aged 7 years. The condition first manifested itself by glandular swelling in the neck. Biopsy revealed the lymphogranulocytic character of the masses. They disappeared under roentgen therapy, but recurred after three months with extensive involvement of the other side of the neck and general enlargement of all superficial lymphatic structures. There was marked enlargement of the liver and spleen. Roentgen therapy again caused almost complete disappearance of the glandular masses but no regression of the splenic enlargements. The case ended fatally with an attack of hemorrhagic pleurisy and bronchopneumonia. At autopsy the changes characteristic of this condition were found in all the involved lymphatic structures and in the liver and spleen.

SCHLUTZ, Chicago.

TAENIA (DIPILYDIUM CANINUM) IN AN INFANT OF THREE MONTHS. GRACIA SCAFFO DE CASAS, Arch. de pediat. d. Uruguay **3**:395 (Sept.) 1932.

The unusual infestation of so young an infant with this form of Taenia is reported. The patient was fed with artificial food (Dryco). Severe diarrhea accompanied the condition and led to severe dehydration and a state of intoxication complicated by convulsive seizures. Taenia canina is commonly found in domestic animals, such as the dog and cat. Fleas and lice from these animals are common carriers of the ova and gain entrance to the child's intestinal tract through contamination of food.

SCHLUTZ, Chicago.

A CASE OF LEINER-MOUSSOUS DISEASE. BERNARDO CARDELLE, Bol. Soc. cubana de pediat. **4**:83 (March) 1932.

The case occurred in an infant 33 days old, weighing 7 pounds and 10 ounces (3,458 Gm.). The treatment, which was according to the method of Montlana, consisted of (1) general desensitization, accomplished by injecting daily some maternal blood serum (or milk), beginning with 0.25 cc. and increasing to 2 cc.; (2) administration of insulin every second day, beginning with 1 unit and increasing to 4, to modify hepatic and pancreatic function, and (3) alteration of the intestinal flora through the daily administration by mouth of anti-enterococcic vaccine.

SCHLUTZ, Chicago.

A CASE OF ENDOCARDITIS LENTA. CARLOS T. GUTIÉRREZ, Rev. de Facultad de med., Bogota **1**:285 (Oct.) 1932.

A case is described in a boy of 14 years. The differential diagnosis is between typhoid fever, tuberculosis, nasopharyngeal infection, endocarditis rheumatica and a low grade leukemia. Diagnosis is made certain by the isolation of Streptococcus viridans from the blood. The slow involution of the disease has lead to a multiplicity of treatment. The author believes that as sulpharsphenamine has some specificity in puerperal streptococcic infections, it might be used to advantage here.

SANFORD, Chicago.

DUODENAL DIVERTICULA AND CHRONIC PANCREATIC DISTURBANCE. W. FULDE, Deutsches Arch. f. klin. Med. **173**:404 (July 25) 1932.

Of ten patients with duodenal diverticula, three had chronic disturbance of the external secretion of the pancreas. The author suggests an etiologic relationship.

DOOLEY, Kent, Conn.

CLINICAL STUDIES OF ALLERGIC DISEASE: IV. BRONCHIAL ASTHMA RESULTING FROM SENSITIVITY TO MOLD SPORES. W. BERGER and K. HANSEN, Deutsches Arch. f. klin. Med. **173**:469 (July 25) 1932.

The preparation of extracts of the various molds is described in detail. In their studies, the authors used Aspergillus fumigatus, niger and glaucus, and Penicillium glaucum. They report fourteen cases of bronchial asthma in which there was pronounced cutaneous sensitivity to one or more of these extracts. Four of these fourteen patients were also sensitive to other allergens. Passive transfer tests were positive in eight of the nine persons studied.

The authors feel that approximately from 8 to 10 per cent of persons with allergic asthma have a practically monovalent sensitivity to molds, and that from 15 to 20 per cent are sensitive to molds in addition to other substances.

DOOLEY, Kent, Conn.

BACTERIOLOGY AND THERAPY OF PNEUMOCOCCUS PERITONITIS. T. ECK and M. GUNDEL, Deutsche Ztschr. f. Chir. **236**:137 (May 17) 1932.

In seventeen cases of pneumococcus peritonitis the authors found type I organisms in sixteen cases and type II c- nisms in one case. In four cases of type I pneumococcus peritonitis in which complete bacteriologic and immunologic studies were carried out, the same organism as to type and virulence was recovered from the peritoneal exudate, blood stream, endocardial fluid, uterus and vaginal secretion. These findings suggested the trial of antipneumococcus serum. In two cases of children of 8 and 5 years, respectively, in which the prognosis seemed very unfavorable, the intravenous and intramuscular administration of antipneumococcus serum caused a rapid and striking improvement; in spite of severe and diffuse peritonitis with accompanying septicemia, both children recovered. This result, the authors believed, could be attributed only to the use of specific serum. They urged that in pneumococcus peritonitis the type of organism should be determined and the homologous antiserum be employed.

GLASER, Rochester, N. Y.

A CASE OF ISOLATED SPONTANEOUS LEVULOSURIA IN A YOUNG CHILD. A. FISCHER, Jahrb. f. Kinderh. **131**:341 (May) 1931.

This is the first reported case of the kind in a child of 2½ years. Levulose was absent in the serum when the patient was fasting. After ingestion of 45 Gm. of levulose, the blood content of levulose increased, but the dextrose content was unaffected. Insulin had no effect on the "levulose curve" of the blood. After ingestion of 50 Gm. of dextrose, the blood-dextrose curve was of the normal type. After subcutaneous injection of epinephrine hydrochloride, small quantities of levulose appeared in the blood.

CLAUSEN, Rochester, N. Y.

BRONCHOGRAPHY AND BRONCHIECTASIS IN CHILDREN. N. A. PANOW and A. M. GELFON, Jahrb. f. Kinderh. **131**:348 (May) 1931.

Iodized poppy seed oil 40 per cent was introduced by means of a rubber catheter through the anesthetized larynx. The method proved of value in children suspected of having bronchiectasis. Careful details of the method and results are given.

CLAUSEN, Rochester, N. Y.

NASAL BREATHING. H. SECKEL, Jahrb. f. Kinderh. **133**:163 (Oct.) 1931.

The author describes a simple pneumographic method for registering the movements of the alae nasi, and distinguishes two respiratory types: the preinspiratory and the expiratory. In the former, the nostrils expand before the chest does; it is observed in a quiet and in an agitated form, in various pathologic conditions of the lungs and in paralysis of the respiratory muscles. The expiratory type occurs in crying and in deep breathing. In dyspnea of febrile, cardiac or nervous origin, nasal movements do not occur. Expiratory nasal breathing originates in nasal reflexes. The preinspiratory type depends on pathologic stimuli in the receptors of the pulmonary automatic regulation.

CLAUSEN, Rochester, N. Y.

ETHYLHYDROCUPREINE IN THE TREATMENT OF CROUPOUS PNEUMONIA IN EARLY CHILDHOOD. PHILIPP LEITNER, Jahrb. f. Kinderh. **135**:257 (May) 1932.

Ethylhydrocupreine was administered as the base, for from three to four times a day for from two to four days, in suppositories containing the following dosage, according to age: under 1 year of age, from 2 to 3 cg.; from 1 to 2 years, from 3 to 4 cg.; from 2 to 5 years, from 4 to 5 cg., and over 5 years, from 5 to 10 cg. In forty-five cases, one death occurred; otitis media developed in three, empyema in two and purulent pericarditis in one. Lysis took place usually within four days. (It is not clear whether this refers to the duration of the entire illness.) The author has no control cases; he reports no results in bronchopneumonia, and compares his results with a reported mortality of 25 per cent in "pneumonia" in childhood.

CLAUSEN, Rochester, N. Y.

THE CIRCULATORY SYSTEM AND THE BLOOD VOLUME IN SICK CHILDREN: I. THE ANEMIAS OF THE FIRST TWO YEARS. H. SECKEL, Jahrb. f. Kinderh. **136**:33 (June) 1932.

The blood volume was determined by the use of trypan red. In the newly born period, the initially high cell volume falls, as do the red cell count and hemoglobin, resulting in the physiologic anemia of early life. The volume of the blood increases in almost direct proportion to the weight of the body. In sixteen cases of anemia the volume of blood was determined; this was done at frequent intervals in eleven patients. It is often diminished. The lowered cell volume is in part compensated by an increase in plasma volume. The effect of transfusion is discussed, and certain examples of unusual types of anemia are presented.

CLAUSEN, Rochester, N. Y.

TREATMENT OF DIABETES IN CHILDREN. E. WALENTA and M. TRUSEN, Monatschr. f. Kinderh. **54**:185, 1932.

Diabetes in children tends to be progressive. If neglected for from one to two years after its diagnosis, it reaches the state designated as "total diabetes" in which there is no hope of recovery of pancreatic function. For this reason, treatment should be started immediately on diagnosis and with a view to making the child sugar-free as soon as possible. A child from 2 to 4 years old should receive 60 calories; a child from 4 to 8 years, from 40 to 50 calories, and a child over 8 years, from 30 to 40 calories, per kilogram of body weight. One third of the calories should be in carbohydrate and two thirds in fat. Only a little protein should be given, namely, from 0.3 to 0.5 Gm. of animal protein per kilogram of body weight. From the first day, insulin should be used in three injections a day, and the dosage should be increased until the child has become sugar-free. As the tolerance of the child increases, the dose of insulin may be reduced. During incidental infections, even without fever, the child should be carefully watched, as sugar tolerance will be found sharply reduced.

When the condition has reached the stage of total diabetes, the writers have secured the best results by placing the child on a mixed diet and giving about 30 to 70 units of insulin daily to insure proper nutrition.

GERSTLEY, Chicago.

TREATMENT OF PYURIA WITH SOY BEAN FEEDINGS. A. MADER, Monatschr. f. Kinderh. **54**:212, 1932.

In treating sixteen infants with acute pyuria, the writer obtained good results by substituting soy bean gruel for milk. The idea back of this is that the soy bean contains the amino-acids, lysine, tryptophan and cystine, which are lacking in milk, while the gruel also alkalinizes the urine. GERSTLEY, Chicago.

LIPOMATOSIS OF THE PANCREAS IN A CHILD. W. HANTELMANN, Virchows Arch. f. path. Anat. **282**:630, 1931.

A boy, aged 9, died of general amyloidosis due to cervical lymphogranulomatosis. He was not obese, and there was no sugar in the urine. At necropsy, the pancreas was found to be enlarged, owing to adipose tissue, which had replaced much of the acinar tissue. The islets had persisted unchanged. Although fatty infiltration of the pancreas is common in adult obese persons, especially those with diabetes, Hantelmann could find only three previously reported cases of a similar condition in children. In none was there obesity, diabetes or detectable disturbance of function due to loss of the external secretion of the pancreas. He ascribes the replacement of pancreatic tissue by fat in this case to a slowly progressing inflammatory process. SCHULTZ, Evanston, Ill. [ARCH. PATH.]

CONGENITAL ABSENCE OF PARATHYROID BODIES. R. RÖSSLE, Virchows Arch. f. path. Anat. **283**:41, 1932.

Following discussion of the more usual maldevelopments of branchiogenic origin, Rössle presents two examples of absence of the parathyroid bodies, as determined by serial sectioning of the tissues of the neck. One was found in an anencephalic infant who lived nine hours; the other, in a female infant with no external malformations who lived ten weeks. Symptoms began at the age of 6 weeks and were those of severe spasmophilia. Necropsy revealed the absence of the substernal portion of the thymus and of the isthmus of the thyroid gland. No parathyroid tissue could be found on serial sectioning of the cervical tissues. The second case offers proof that infantile tetany may be due to deficient function of the parathyroid glands. SCHULTZ, Evanston, Ill. [ARCH. PATH.]

PAGET'S OSTEITIS DEFORMANS. G. SCHMORL, Virchows Arch. f. path. Anat. **283**:694, 1932.

In 1926, Schmorl expressed the opinion, which was in accord with the then prevailing view, that Paget's osteitis deformans and von Recklinghausen's generalized osteitis fibrosa are phases of the same disease. In 1930, as the result of study of a much larger material, he announced the belief that the diseases have nothing in common. This conception, which forms the basis of the present profusely illustrated and detailed histologic description of osteitis deformans, is based on 190 cases of Paget's disease, 138 of which Schmorl collected between March, 1926 and the end of 1930 in the course of examinations of the skeletal system at necropsy. The cases were encountered in a total of 4,614 necropsies of persons over 40 years of age, an incidence of 3 per cent. Schmorl has never seen Paget's disease in a person under 40 years of age. The disease occurred in 3.5 per cent of men over 40 years old who were examined post mortem and in 2.5 per cent of women. The disease was never generalized, although involvement of more than one bone was noted. The chief sites of localization, with the percentages, were: sacrum, 56.5; vertebral column, 50; right femur, 31.2; skull, 28.3; sternum, 23.2;

pelvis, 21.7. Histologically characteristic of Paget's disease is the mosaic structure of the involved bone. This picture is due to variously shaped and sized areas of old and new-formed bone separated from each other by a ground substance staining blue with hematoxylin. The blue-stained material is bone undergoing lacunar resorption. Contrary to the opinion of previous investigators and contrary to what occurs in von Recklinghausen's disease, the marrow is normal in the early stages of the disease. Bone resorption and bone formation occur in both spongy and compact bone. Localized areas of fibrosis appear in time in the marrow of the spongy bone; these become transformed into fibrous bone. In the compact bone, the process begins within the central portion with the presence of one or more osteoclasts in the haversian canals. Bone resorption by these cells leads to the formation of spaces in which bone formation and bone resorption proceed rapidly, bone formation usually predominating. During the active stage the bone is incompletely calcified, but may become completely calcified when the process comes to rest. The overproduction of bone is held to be compensatory to the weakening of the bone caused by resorption and by the formation of new bone at such a rate that it cannot be completely calcified before it is in turn partly resorbed. The periosteum may form a layer of dense bone or osteophytic elevations of fibrous bone. The gross and microscopic appearances may be complicated by osteoporosis and bone atrophy, which are not infrequent in elderly patients with Paget's disease. Schmorl has never seen the combination of osteitis deformans with osteomalacia. The cause of the disease is not known. The calcium metabolism appears to be normal; complete calcification of the newly formed bone as soon as the process of resorption ceases is evidence that the process is not one of deficient calcium deposition. Schmorl has paid particular attention to the parathyroid bodies in his cases; he has never detected any abnormality in them. A concluding section of the paper gives a concise description of the gross and histologic differences between Paget's osteitis deformans and von Recklinghausen's osteitis fibrosa, which can no longer be considered the hyperostotic and the hypoostotic forms of a single disease for which Christeller proposed the name osteodystrophia fibrosa.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

A CASE OF FAMILIAL CIRRHOSIS OF THE LIVER WITH HYPOGLYCEMIA. T. HALBERTSMA, Ztschr. f. Kinderh. **53**:295, 1932.

The author reports that in a family in which three children had large livers, one, a girl of 6, had attacks of hypoglycemia. Clinically, there were splenohepatomegaly, ascites and urobilinuria. The blood sugar was as low as 0.016 Gm. per hundred cubic centimeters, and the levulose tolerance test was abnormally high. The child died suddenly, and at autopsy the liver was found to be extremely atrophic (Laënnec's cirrhosis). The other two children are still living. One has a very large, smooth liver and the other a smaller but firmer organ. Their blood sugar values during fasting are within normal limits.

SHELLING, Baltimore.

Nervous Diseases

CELLULAR INCLUSIONS IN CEREBRAL LESIONS OF LETHARGIC ENCEPHALITIS. JAMES R. DAWSON, JR., Am. J. Path. **9**:7 (Jan.) 1933.

Inclusion bodies within nerve cells and neuroglial cells comparable to those of herpes simplex, varicella and virus III disease of rabbits were found in one of three cases of lethargic encephalitis. On the basis of this difference and other variations in symptoms and pathologic findings, it is suggested that lethargic encephalitis is not a clinical or pathologic entity. Animal inoculations with material from all three cases gave negative results.

MOORE, Cleveland.

STATUS MARMORATUS: ETIOLOGY AND MANNER OF DEVELOPMENT. K. LÖWENBERG and WILLIAM MALAMUD, Arch. Neurol. & Psychiat. **29**:104 (Jan.) 1933.

Status marmoratus is a name given to a disease syndrome in which the microscopic neuropathologic preparation has an alteration of light and dark areas resembling marble. The myelin sheath preparations show, besides the normal myelin, a quantity of irregular, darkly stained condensations, blotches and stripes, forming a network. These darkly stained structures are fine, delicate, myelinated fibers. The remainder of the striatum is more or less destroyed. The concomitant clinical picture has been described as showing itself at, or soon after, birth. It consists of spasticity, peculiar postures of the extrapyramidal type, athetoid movements and convulsive paralysis. Less characteristic findings are convulsive laughing or crying, nystagmus, convulsions and mental defect. In some cases other members of the family were thought to have similar clinical findings. This, with the early development, led to the hypothesis that it was a developmental anomaly.

In studying three cases the author found an irrelevant family history and a period of normalcy between birth and development of the symptoms. Pathologic evidence is presented that normal development of the brain preceded the pathologic changes, and that changes may occur in other parts of the brain than the basal ganglions, as originally stressed. The authors conclude that the whole picture may be explained as an encephalitic process, and that the condition is therefore most probably acquired.

BEVERLY, Chicago.

THE SPECIFIC PROPHYLAXIS OF PNEUMOCOCCUS AND STREPTOCOCCUS MENINGITIS: II. VACCINE PROPHYLAXIS. JOHN A. KOLMER and K. W. AMANO, Arch. Otolaryng. **15**:547 (April) 1932.

Because of the seriousness of meningitis complicating surgical cases of chronic sinus infections and otitis media, a study was made of the two most common organisms in meningitis of this origin, namely, pneumococci and streptococci, in order to see if immunity could be induced by an autogenous vaccine before operation. Rabbits were used, and the vaccines were administered by intracutaneous, subcutaneous, intravenous and oral (two different dosages) methods. After what was considered sufficient treatment, these animals along with suitable controls were inoculated to produce meningitis.

It was found that: "1. It is possible to raise the resistance of rabbits to meningeal infection with virulent pneumococci and streptococci by preliminary immunization with autogenous vaccines. 2. Especially encouraging results were observed among rabbits vaccinated with type I pneumococcus and later inoculated intratympanically with the same strain. 3. With types II and III pneumococci and Streptococcus haemolyticus vaccines, the effects of immunization were less apparent when the animals were later inoculated intracisternally with virulent cultures producing fulminating meningitis among the controls. 4. The intracutaneous injection of pneumococcus and streptococcus vaccines appeared to produce a higher degree of immunity than the subcutaneous injections. 5. The oral administration of pneumococcus vaccines sometimes resulted in producing a high degree of resistance to meningeal infection. 6. It is recommended that when time permits careful bacteriologic examination of the secretions be made in chronic sinus and otitic infections, especially ethmoiditis, and that in pneumococcus and streptococcus infections autogenous vaccines be administered preliminary to operative procedures to raise immunologic resistance when meningitis is feared as a possible complication."

BARNETT, Chicago.

BIOGRAPHICAL RECORDS OF MEMORY IN PRE-SCHOOL CHILDREN. E. B. HURLOCK and R. SCHWARTZ, Child Development **3**:230 (Sept.) 1932.

Biographical records were analyzed to determine how the memory of the normal child in a normal environment grows during the first six years of life, as well as to determine how the latency period or "the interval elapsing between the

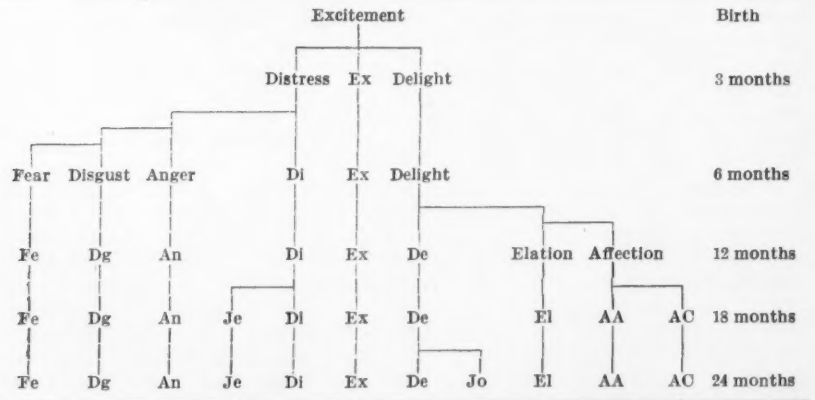
occurrence of an event and the memory of it," lengthens with the age of the child. The investigators conclude from their researches that in the first half year of life there appears memory of an impressionistic type, whereas memory of the true type appears by the end of the first year and is aroused only by sensory stimuli. By the end of the second year, sensory stimuli are no longer necessary, as memory develops to more ideational varieties of experience. Memory is stronger during the first two years for persons and objects than for situations, but from 3 to 6 years the memory of persons and objects in situations become significant factors. A longer latency period was found for unusual events and things of interest than for the more neutrally toned events. Recognition and remembrance of colors and forms appears in the second half of the third year. At 3 years, the child is able, after the lapse of a few days, to recount a story heard and give a detailed account of past experiences. No accurate idea of time is present even up to 6 years of age. The latency period increases in length from birth to 6 years as follows: first year, five days; second year, from two to three weeks; third year, from two to three months; fourth to sixth year, one year with a maximum of three and one-half years.

ABRAMSON, New York.

EMOTIONAL DEVELOPMENT IN EARLY INFANCY. KATHARINE M. BANHAM BRIDGES, Child Development **3**:324 (Dec.) 1932.

The emotional behavior of sixty-two infants in the Montreal Foundling and Baby Hospital was observed and recorded over a period of from three to four months. The data were then analyzed from the point of view of development from age to age. The author summarizes her results in the following schematic form:

Table Showing Approximate Ages of Differentiation of Various Emotions During the First Two Years of Life



AA = affection for adults; AC = affection for children; An = anger; De = delight; Dg = disgust; Di = distress; El = elation; Ex = excitement; Fe = fear; Je = jealousy; Jo = joy.

In the discussion, Bridges again stresses the gradual evolution of the emotions from birth onward, the earliest reactions being general and poorly organized, assuming a more definite form in relation to more specific stimuli only after the process of differentiation.

ABRAMSON, New York.

ADULT ADJUSTMENTS AND NONADJUSTMENTS IN RELATION TO THEIR EFFECTS UPON CHILDREN. S. W. HARTWELL, Ment. Hyg. **16**:598 (Oct.) 1932.

Hartwell discusses the influence of adult attitudes on the behavior of children, stressing the influence of environment, intellectual capacity and bodily health as

factors in the past which have created within us feelings or emotions contributing to the sum total of our personalities. Success as a parent is dependent, first, on ability to act as a protector of the child and, secondly, as an interpreter. Thus, it is necessary for the adult to understand his own personality and his own feelings in order to avoid making mistakes in the rearing of his own children. The behavior of the child reflects or mirrors adult attitudes and feelings. The interpretation of these reactions are among the most vital experiences the child will ever have.

ABRAMSON, New York.

AGE, A FACTOR IN THE INCREASE OF MENTAL DISORDERS. E. B. WINSTON, Ment. Hyg. **16**:650 (Oct.) 1932.

The author calls attention to the well known relationship between age and the incidence of mental disease and to the fact that mental diseases become more numerous with advancement in years. More than four times as many persons enter hospitals for mental diseases at the age of 80 as do at the age of 20. Winston presents the following table to illustrate the aging of the population of the United States:

Percentage Age Distribution, 1900 to 1930

Age Group	1900	1910	1920	1930
Under 15 years	34.4	32.1	31.7	29.4
15 to 24 years	19.6	19.7	17.7	18.3
25 to 44 years	28.0	29.1	29.6	29.4
45 to 64 years	13.7	14.6	16.1	17.4
65 years and over	4.0	4.3	4.7	5.5

Whelpton's predictions of the age groupings of the population of the United States over a period of 55 years, i. e., from 1920 to 1975, were utilized to determine the effect of advancing age distribution on the mental health of the country. Winston concludes that "if all other conditions should remain the same during the next fifty years, on the basis of age alone there would be an increase of from 6 to 7 per cent in the rate of admissions to hospitals for mental disease, owing to the gradual and inevitable aging of the population." This statement would be true despite the effects of mental hygiene measures which would exert greater influence in a younger population.

ABRAMSON, New York.

THE MENTAL HEALTH OF CHILDREN: A PEDIATRIC RESPONSIBILITY. HORTON CASPARIS, South. M. J. **26**:7 (Jan.) 1933.

Mental and physical health of children cannot be dissociated, and mental health should be just as much the concern of the pediatrician as is the physical health of children. This is especially true in the pediatric field of preventive medicine, since there is a growing tendency to place the child under pediatric supervision from birth.

As the responsibility for the training of the child largely rests with the parents, the pediatrician should give them genuinely sympathetic and constructive suggestions as to the proper methods to pursue.

The establishment of habit formation, avoidance of overanxiety on the part of the parents, proper handling of tantrums and the furnishing of good examples of reliability, responsibility, courage and confidence are some of the phases of child training about which the pediatrician should concern himself and advise the parents. Psychiatrists and psychologists who have concerned themselves with children can be of invaluable aid to pediatricians in their own training and as consultants in their practice.

SCHLUTZ, Chicago.

TORSION-SPASM (DYSTONIA LENTICULARIS). HUGH G. GARLAND, J. Neurol. & Psychopath. **12**:193 (Jan.) 1932.

A Jewish boy, aged 17, had become ill in the spring of 1918, at the age of 5, with malaise, tremor and weakness of the right hand, dysarthria and difficulty in standing. His condition improved in the next two years, but thereafter became worse, with weakness of hemiplegic distribution, severe involuntary spasms, marked kyphoscoliosis, wasting of the right arm and leg, cogwheel rigidity, spasmodic breathing and slight pupillary irregularity with nystagmoid jerks. A Babinski sign had appeared recently, without reflex changes. The patient had been operated on for contracture of the tendo achillis. There were no sphincteric, sensory or intellectual disturbances. The author believes that this is a case of torsion spasm, with involvement of the pyramidal system, but could not exclude a possible post-encephalitic manifestation.

SPERLING, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

TUMORS OF THE HYPOPHYSEAL REGION TREATED BY RADIOTHERAPY. PARFONRY, Ann. d'ocul. **169**:651 (Aug.) 1932.

Parfonry reports three cases in which tumors of the hypophyseal region were treated with radiotherapy (in two for ten years, in the other for four years) and in which improvement in the general condition, visual fields and visual acuity was maintained throughout this period. He concludes from his observations that, although surgical treatment is important, it should be remembered that radiotherapy is of value when operation cannot be performed.

Morax reported one case in which treatment was given with radiotherapy twenty times. Visual acuity was maintained for seven years. Dupuy-Dutemps had previously reported several cases which he had followed for more than five years. In his opinion, radiotherapy should always be given a trial before operation is advised. Magitot emphasized the fact that in one of the cases presented the visual field of one eye, which had been completely abolished, was totally restored. He also stated that in certain decompressions of the chiasm Cushing had seen the visual field restored on the operating table. Sourdille reported that he preferred operation. Bollack had previously reported five cases in which the condition was favorably influenced by radiotherapy, but he believes that operation offers the best chance for recovery.

BERENS, New York. [ARCH. NEUROL. & PSYCHIAT.]

PATHOGENESIS OF MONGOLISM. K. RACHID, Arch. de méd. d. enf. **36**:30 (Jan.) 1933.

In a study of four cases of mongolian idiocy at Stamboul, Rachid was impressed, as all clinicians have been, with the unvarying syndrome that characterizes this peculiar disorder.

In one of these cases the condition appeared to be associated with cretinism, and in view of the accepted belief that the latter is always a sequel to congenital hypoplasia of the thyroid, the idea presented itself that mongolism, on account of its unchanging character, may also be explained on the basis of a congenital, ulcerative agenesia. The author expresses the hope that glands of internal secretion, as yet unknown, may hold the key to the pathogenesis of this mysterious condition.

AMESSE, Denver.

MENINGOCELE OF THE UPPER THORACIC REGION IN A NEW-BORN INFANT SUCCESSFULLY TREATED BY OPERATION. GRANDCLAUDE, R. PALLIEZ and L. GERNEZ, Bull. Soc. d'obst. et de gynéc. **21**:474 (July) 1932.

The mother had previously had two normal infants, and the family history was unimportant. The child in the case reported was a boy, normally delivered, who weighed 3,350 Gm. He presented no abnormality except a swelling, the size

of a small orange, situated at the level of the fourth thoracic vertebra. The swelling was cystic, with a violaceous color and a sessile base. The tumor showed fluctuation, could not be reduced and was not changed in character when the infant cried. It was transilluminated well. The general appearance was that of a little cup inverted between the shoulder blades. A roentgenogram showed no abnormality of the spinal column. The cyst was easily excised, being connected to deeper structures only by a fibrous cord. It contained a clear liquid having the appearance of cerebrospinal fluid. Histologically the membranes lining the cyst resembled those lining the cerebrospinal cavity. Structures resembling pacchionian bodies were found. There was no tissue of nerve origin. Cysts of this nature are unusual. The infant made an uneventful recovery and was well when seen six months later.

GLASER, Rochester, N. Y.

"NEUROPATHIC" ARTHRITIS OF THE KNEE IN A GIRL WHO HAD BEEN OPERATED ON FOR SPINA BIFIDA. L. BABONNEIX and L. LAMY, Bull. Soc. de pédiat. de Paris **30**:26 (Jan. 19) 1932.

A girl, 4½ years old, had a swollen right knee with effusion. Roentgen examination showed bony changes at the ends of the femur and tibia and in the center of ossification for the patella. The right lower extremity was longer than the left. The child had a congenital dislocation of the left hip and a spina bifida which was operated on when she was 2 years old. She was never able to walk. There was no evidence of tuberculosis or syphilis, and because of the lack of the usual inflammatory phenomena associated with an infective arthritis the condition is regarded as "neuropathic."

BENJAMIN, Montreal, Canada.

STAPHYLOCOCCIC ABSCESS OF THE BRAIN WITH UNILATERAL CRANIAL DILATATION AND EXOPHTHALMOS IN AN INFANT SIX MONTHS OLD. E. LESNE, Y. BERTRAND and J. CAROLI, Bull. Soc. de pédiat. de Paris **30**:39 (Jan. 19) 1932.

A healthy infant began to show a deformity of the left side of the head at the age of 3 months. This progressed slowly, and when admitted to the hospital at the age of 6 months the child showed marked dilatation of the left half of the cranium with all the sutures open, especially that between the frontal and parietal bones, and the left half of the anterior fontanel dilated and bulging. The left eye was pushed downward and forward. There was no fever, vomiting, cries of pain or convulsions. The leukocyte count was normal. A trocar inserted through the wide-open frontoparietal suture to a depth of about 2 cm. yielded a xanthochromic fluid which coagulated into a solid mass that contained no organisms and gave a negative culture, but at a depth of about 4 cm. pus was obtained from which virulent Staphylococcus aureus was grown. The infant did well for ten days after this exploratory puncture, but then began to have marked pyrexia and dyspnea and died after eight days of high temperature. Necropsy showed bronchopneumonia and areas of fatty degeneration of the liver, but the brain was the chief point of interest. On the left side there were a large area of softening between the frontal and temporal lobes and a large abscess with a dense fibrous capsule around it. No portal of entry for the formation of the abscess was found. Histologically there was a dense neuroglia sclerosis about the abscess, giving the appearance of a tumor, and cystic degeneration of the softened subcortical area with thrombosis of the arteries in this region.

BENJAMIN, Montreal, Canada.

THE PROBLEMS AND RESULTS OF THE INSTITUTIONAL CARE OF PSYCHOPATHIC CHILDREN. ADALBERT GREGOR, Ztschr. f. Kinderforsch. **40**:291 (Aug. 19) 1932.

Gregor, who is the director of the Reform School at Flehingen (Baden), has studied the subsequent careers of one hundred children who were in his institution and who had been released previous to 1925. Only eight of these patients could

not be traced. Sixty boys had adapted themselves and established a reputable relation to society; twenty-one had returned to a criminal or asocial career. In ten cases the future of the child was still in question.

The author is, therefore, of the opinion that the reeducation in Flehingen was of great value. The vicious cycle of juvenile crime, bad reputation and asocial tendencies was broken, and the children were given an opportunity to establish a new relationship with the community. Gregor was particularly interested in the causes which brought about a failure of this training. He finds by a study of the individual cases that the prognosis depends on the original character of the child and not so much on his previous environment or experiences. The most important factor is the "moral constitution" of the pupil, which depends not only on the temperament but also on the will power. An inferior moral constitution is shown by a lack of temperament, an absence of sympathy and a stolid, indifferent, egocentric autistic character.

It is therefore of importance that the applicants for a reform school be carefully examined before admittance, and that those children who have a promising character be given preference. At a time when financial retrenchment is so necessary, the small sums available for the reform schools should not be wasted on hopeless cases.

Gregor finds that the after-care of his discharged pupils is of great importance in preventing a relapse into their previous habits at critical moments. This is particularly true at the present time, since there is practically no prospect of work for such persons. It is obvious that this after-care cannot be given by the institution itself but must be left to other organizations such as charitable societies, religious bodies, schools and physicians.

REICHLE, Cleveland.

THE CHARACTER OF CHILDREN. HANS HEINZE, Ztschr. f. Kinderforsch. **40**:371 (Sept. 21) 1932.

This article is particularly concerned with the problem of temperament as opposed to intelligence in the child. The author uses the German word *Gemüt* and says that it is a spiritual characteristic present as a natural disposition in different degrees in different persons which can be developed or neglected but which cannot be learned or taught. He quotes many well known psychologists and psychiatrists, such as Bleuler, Kornfeld and Birnbaum, in maintaining his belief that temperament may be entirely independent of the degree of intelligence. In other words, he accepts the concept of "moral insanity" and ascribes this not so much to mental deficiency as to lack of feeling. He points out that there have been many instances in history of very intelligent persons whose moral lives have been exceedingly deplorable. The misunderstandings which have been aroused by this problem he ascribes to the fact that an intelligent psychopathic person may develop a rationalized set of morals; without any ethical background he learns to realize that his adaptation to certain moral standards is of practical advantage to him. These persons have ethical knowledge but no ethical feelings. On the other hand, experienced physicians and psychologists know many children who are mentally deficient but whose wealth in temperament gives them a strong ethical background.

On the basis of such conceptions, Heinze has studied twelve children presenting behavior problems who were brought to the Psychiatric Clinic in Leipzig. He divides them into two groups: six who were natively poor in temperament and six whose temperamental life had been blunted by previous experiences. In the latter cases the institutional training proved to be of great value, whereas the first group resisted all treatment.

The author, therefore, comes to the conclusion that the education of children suffering from behavior problems depends not only on the intelligence and the previous environment but on the sensitivity of temperament.

REICHLE, Cleveland.

THE LEGAL INSIGHT OF JUVENILES. SIEGFRIED FISCHER, Ztschr. f. Kinderforsch. **40**:497 (Nov. 3) 1932.

The new criminal laws for juveniles in Germany exclude from punishment such acts as have been carried out at a time when the agent was incapable of recognizing the criminal nature of the act or lacked the will power to act in conformity with his knowledge. The author points out that psychologists have not yet studied the legal insight of juveniles, their ability to differentiate between morality and legality. He suggests, therefore, that a more extensive investigation is necessary in order to aid the judicial authorities in settling problems aroused by the new laws for juveniles.

REICHLE, Cleveland.

EFFECTS OF SEXUAL ATTACKS UPON THE CHARACTER OF YOUNG GIRLS. J. MOSES, Ztschr. f. Kinderforsch. **40**:542 (Nov. 3) 1932.

Both for theoretical and practical purposes, it is important to discover whether a sexual attack before puberty will have a permanent effect on the character of a young girl. The author has observed sixty children from the ages of from 4 to 14. He calls attention to the work of Goroncy, who examined twenty-four women over 20 years who had been attacked before the age of 14. Goroncy found that the event had been forgotten in a large number of cases, and that in general it had practically no effect.

Moses has come to different conclusions. He believes that this discrepancy is due to the fact that he examined the girls shortly after the attacks, when the memory of this event was still fresh in their minds. His children are not typical of a cross-section of the population, since many of them, twenty-one of sixty, were mentally deficient, and most of the remainder came from low social classes. Twenty-three of the sixty girls showed no unfavorable effects, and in thirty-seven cases in which premature sexuality had occurred it was difficult to be sure that this was not due to constitutional conditions which may have been present before the sexual trauma. In fact, the question arises as to whether or not such persons are predisposed to sexual attacks.

REICHLE, Cleveland.

ABSCESSES OF THE BRAIN. W. KLESTADT, Ztschr. f. Laryng., Rhin., Otol. (Teil 1: Folia oto-laryng.) **23**:94 (Sept.) 1932.

Klestadt reports three cases of abscess of the brain in which necropsies revealed conditions that were unexpected on the basis of the clinical symptoms. The first case concerned a boy with otogenous sinus thrombosis and an abscess of the temporal lobe and another in the cerebellum. About five weeks after closure of the wounds of the thrombophlebitis and the cerebellar abscess, when the fistula, which had persisted in the abscess of the temporal lobe, was finally healing, a temporal lobe syndrome appeared on the right side. The fistula was reexamined, but yielded no pus. Meningitis set in. Search for an abscess and attempted drainage of the inferior cornu of the lateral ventricle and the posterior cornu were in vain. The case terminated fatally. At necropsy, a scar 3 cm. in length was found in the cerebellum. No suppuration was found in the brain except that due to the last interventions. The author thinks that the new focal symptoms were probably due to the effects of cicatrization, and that the boy would have survived had it not been for exacerbation of the meningitis caused by the search for the abscess. The second case concerned a man with severe aphasia following acute otitis media, who died of meningitis. At necropsy, the author expected to find a large abscess, because the aphasia had included practically all varieties, but instead the original abscess was only the size of a walnut. Since the marked regression of aphasic symptoms which followed cerebral decompression and drainage of the abscess had been followed by a recurrence of these symptoms, the author expected a severe retention of pus or a focally exacerbated encephalitis, but he found, instead, only a small, cherry-sized abscess near the major abscess, but

independent of it. The third case concerned a girl with an otogenous meningitis. Radical operation exposed an extradural abscess extending from the upper bend of the sinus toward the median cranial fossa. At necropsy, a large, oval, subdural abscess was found ending about 1 cm. behind the trepanation opening and not connected with the region of the extradural abscess. It extended from the temporal lobe backward over a considerable part of the occipital lobe. The lack of focal symptoms and the general course of disease justified the conservative intervention.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

Diseases of the Eye

CHOKING OF THE OPTIC DISKS IN DISEASES OTHER THAN TUMOR OF THE BRAIN. JOHN T. STOUGH, Arch. Ophth. **8**:821 (Dec.) 1932.

In making a diagnosis of intracranial tumor, the physician seeks the presence of what is known as choking of the optic disk. Evidence favors the view that it is due to an obstruction of the internal flow of blood from the retina, with perhaps also obstruction of the lymphatic drainage of the retina. If the ophthalmologist could always be certain of the diagnosis of choking of the optic disks, and if this finding were produced only by intracranial tumor, it would be helpful. Unfortunately, choking of the optic disks may be simulated by other conditions of the retina, and actually produced by diseases other than intracranial tumor. The author, as all ophthalmologists, reports cases of definite choking of the optic disks with other symptoms suggestive of intracranial tumor in which the subsequent course of the disease seemed definitely to rule out this diagnosis. These included cases of optic neuritis, cases due to infection about the teeth or the sinuses, the retinitis of cardiovascular renal disease and cases of hypertension without marked renal or cardiac lesions, in which the fundi presented a picture identical with that of choking of the optic disks with increased intracranial tension.

In some of the cases, especially those accompanied by cerebral arteriosclerosis with bilateral choking of the optic disks, the symptoms of the head were so definite that ventriculograms and special pictures were taken. Naturally, all of them showed normal conditions.

In one case of acute lead poisoning, the neurologist stated that he was of the opinion that an intracranial tumor was present. In three other cases, no definite diagnosis was ever made as to what the cause of the choking was. In one case, that of a child, aged 4 years, a neurologic examination revealed a cracked-pot resonance of the head, hypotonia of the extremities, decomposition of the movements of the left hand and, at times, a bilateral Babinski phenomenon. This patient also showed a bilateral paralysis of the sixth nerve. The patient had from 3 to 4 diopters of swelling with numerous hemorrhages. Roentgen examination revealed a diastasis of the sutures and digital markings on the inner tables of the skull, pointing to an increase of the intracranial tension without localizing signs of a tumor of the brain. A midline cerebellar tumor was suspected. A suboccipital decompression and cerebellar exploration, however, revealed nothing abnormal. Following this operation, roentgen treatments were given. The patient completely recovered.

Another child, also aged 4 years, with very similar neurologic findings, had a similar exploratory operation. In this case a greatly dilated posterior cistern was discovered, but no tumor. After a rather stormy convalescence, this child also made an uneventful recovery. (It seems to the reviewer that this case could well have been an inflammatory, posterior arachnoiditis.)

The last case mentioned in the series was one in which a diagnosis of bilateral papilledema had been made after an illness of two weeks. Here, also, there were neurologic symptoms: dizziness without loss of consciousness, weakness of both legs and tingling of the right leg. Roentgenograms of the head gave absolutely, negative findings. No operation was performed in this case. The child's fundi,

after a period of six months, showed a rather high degree of atrophy of the bilateral optic nerve, probably of a secondary nature. The author, in his concluding comment, calls attention to the fact that the condition in this case as well was probably inflammatory and could have been one of encephalitis.

SPAETH, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

TUBERCULOSIS OF THE EYE. ALAN C. WOODS, Internat. Clin. **1**:96 (March) 1933.

Intra-ocular tuberculosis is always of hematogenic origin and is usually secondary to a tracheobronchial infection. Tuberculous lesions of the cornea, sclera, iris, ciliary body, choroid and retina are excellently illustrated. The author considers that phlyctenules are an allergic reaction of the conjunctiva and the corneal epithelium due to sensitization to and intoxication caused by tuberculoprotein. A phlyctenule is a mass of epithelioid cells with a few polymorphonuclear leukocytes surrounded by a zone of lymphocytes. Tuberculin therapy is beneficial in ocular tuberculosis.

MILLER, South Bend, Ind.

ETIOLOGY AND TREATMENT OF STRABISMUS. LAURENCE T. POST, J. Pediat. **2**: 448 (April) 1933.

The causes of strabismus in children and the methods of treatment are outlined. Every patient with strabismus should receive careful attention at the onset, because strabismus can be corrected in a large percentage of cases, and because if it is neglected the deleterious effects are far-reaching. Cooperation between the pediatrician and the ophthalmologist is essential for the proper correction of this defect at an early age.

LEMASTER, Evanston, Ill.

VOLUMINOUS ANGIOMA OF THE ORBIT. VILLARD and DEJEAN, Arch. d'opht. **49**:638 (Oct.) 1932.

The authors present a case of marked orbital angioma which is of especial interest not only because of the marked proptosis which it produced but also from several other points of view. The proptosis in the case presented, illustrated by a photograph, made the eyeball appear as though it were hanging by a pedicle from the orbit. The proptosis was first noted when the patient was 3 years old and had slowly progressed until she came for operation at the age of 18 years. Although it was so marked that the lids could not be closed over it even after pressure, the cornea remained unaffected. The orbital mass produced also a high degree of hypermetropia, but the interior of the eye was essentially normal. At operation it was found intimately connected with the optic nerve, which was damaged unavoidably during the removal of the tumor. Histologically, it was found to be made up of large cavernous blood sinuses and large masses of small capillaries, so that it was a combined cavernous telangiectatic angioma. Its removal was accomplished by orbitotomy according to the method of Rollet. The authors believe that the tumor had a congenital origin.

MARLOW, Syracuse, N. Y. [ARCH. OPHTH.]

TUMOR OF THE RETINA WITH MULTIPLE METASTASES. A. MONTHUS and A. FAVORY, Bull. Soc. de pédiat. de Paris **30**:237 (April 19) 1932.

A girl, aged 18 months, had a tumor of the retina of the left eye. The eye was enucleated, and histologic examination of the tumor showed it to be sarcomatous. Ten months later the child presented multiple bony metastases, and it was found that the retina of the right eye had been invaded by tumor tissue.

BENJAMIN, Montreal, Canada.

Diseases of the Ear, Nose and Throat

CHLOROMA: ITS RELATION TO OTOLARYNGOLOGY. ROBERT LEVY and HERMAN I. LAFF, Arch. Otolaryng. **15**:610 (April) 1932.

Chloroma is a rare disease, only 162 cases having been reported up to 1929. It was first described by Burns in 1823. It characteristically invades the cranial bones and their cavities, forming both solid and fluid tumor masses which often have a greenish tint and which simulate suppuration and malignant disease of the afflicted parts. The color gives it the name of chloroma.

The disease is probably a malignant form of leukemia. The white cells resulting from the atypical proliferation have the power of multiplying in the blood stream and in the tissue spaces, thus giving rise to masses of cells having the characteristic features of metastatic tumors; hence the disease is probably a malignant form of leukemia. The tumors form especially in the cranium, the sinuses, the orbits, the lids, the temporal bones and the oral and nasal cavities. Other structures throughout the body are also involved, though less frequently, the bones and bone marrow being favored locations.

Chloroma occurs more frequently in males during childhood. The onset of symptoms is insidious, the symptoms being essentially those of leukemia, malnutrition, weakness, pallor, hemorrhage and pain in the long bones. After the tumors develop, the local symptoms are those referable to the structures involved and the nature of the involvement. The blood findings are variable. The lowest white cell count recorded is 3,200 per cubic millimeter, and the highest, 1,880,000. Brannen states that chloroma is an "unusual form of myelogenous leukemia" and that "aleukemic stages are common, whereas proven aleukemic forms of the disease are very rare." Marked anemia is usually present.

The prognosis is fatal, although some hope is now being entertained for treatment with the x-rays.

BARNETT, Chicago.

DENTAL FOREIGN BODY IN THE AIR PASSAGES. JULIAN L. ROGATZ, Arch. Pediat. **50**:18 (Jan.) 1933.

The author urges that early roentgenography and bronchoscopy be utilized in the effort to ascertain the presence of a forgein body suspected from the history and physical signs, in order to assure a favorable prognosis in what might otherwise prove to be a fatal case. He calls attention to the danger of aspirated dental material and reports a fatal case in which a child aspirated a molar tooth.

The literature concerning foreign bodies in the air passages is reviewed, and the symptomatology is discussed.

WADDELL, JR., University, Va.

STUDIES IN CHRONIC SINUSITIS IN CHILDREN. J. S. UHR and J. W. PUGH, J. Pediat. **2**:418 (April) 1933.

Children complaining of frequent colds were examined carefully for signs of chronic sinusitis, which was frequently found. The case histories of eighteen patients are presented. A definite connection was seen between chronic nasopharyngitis and chronic sinus infection in children. Marked improvement followed treatment, which was planned to be as simple as possible, depending on the pathologic conditions. The authors state that they are convinced of the value, indeed the necessity, of the proper surgical treatment when pus is present, for "where there is pus, there should be drainage."

LEMASTER, Evanston, Ill.

ACUTE OTITIS MEDIA IN INFANCY. N. ASHERSON, Arch. Dis. Childhood **7**:159 (June) 1932.

The author (a surgeon for diseases of the ear, nose and throat), in a study of acute otitis media in infants, describes the anatomy of the middle ear and the mastoid. He reports several cases of purulent otitis media in new-born infants. In

these cases the symptoms are usually: (*a*) fever of unknown origin, (*b*) obvious earache, (*c*) a discharge from the ear or (*d*) signs suggestive of meningitis. The tympanic membrane may appear to be normal, and still there may be pus deep in the middle ear. In cases of acute otitis media in which the temperature is 100 F., myringotomy should be performed. In cases of infantile gastro-enteritis, the ears should be observed frequently. If myringotomy reveals pus, the antrum should be drained.

SAPPINGTON, San Francisco.

THE FOREIGN BODY IN THE FOOD OR AIR PASSAGE. D. A. CROW, Practitioner **130**:369 (March) 1933.

Crow strongly urges that all foreign bodies in the esophagus which do not naturally pass down in six hours be removed by an experienced esophagoscopist. The degree of urgency depends somewhat on the sharpness of the swallowed object, since the wall of the esophagus is so thin that a pin or a bone may work its way through in a short time and may be detected only after a mediastinal abscess has formed. In the case of a foreign body in the air passage (except when complete laryngeal obstruction has occurred) the procedure is as follows: (*a*) the taking of a careful history, with special reference to the cough at the moment of inspiration; (*b*) an indirect laryngeal examination; (*c*) a thorough physical examination of the chest; (*d*) examination with the x-rays and (*e*) by bronchoscopy. Except in cases of almost complete obstruction, immediate bronchoscopy is not essential, as the trachea and bronchi are cartilaginous tubes and are not liable to instant perforation. Instructions for incising the cricothyroid membrane to relieve the complete blockage of air are given in detail.

The author believes that a foreign body in the bronchial tubes will seldom be coughed up; hence more than a short delay before examination by bronchoscopy is not justified.

In regard to prophylaxis, the following suggestions are made: 1. Pins, nails, coins and other articles should not be held in the mouth. 2. Dentures should fit properly. 3. Whooping cough and postanesthetic vomiting should be carefully treated. 4. The posterior part of the pharynx should be protected when an anesthetic is given for dental extraction.

KELLY, Milwaukee.

ACUTE LARYNGEAL CROUP AND ATMOSPHERIC CHANGE. H. VON NORDENSKJOLD, Arch. f. Kinderh. **98**:211 (Feb. 21) 1933.

The author confirms de Rudder's view that weather conditions have a bearing on the occurrence of certain illnesses. Nineteen of twenty-four cases of laryngeal croup occurred at times of marked atmospheric change.

LEMASTER, Evanston, Ill.

METASTATIC CEREBRAL ABSCESSES IN OTOGENOUS PYEMIA IN A CHILD AGED NINE YEARS. I. HOFER, Ztschr. f. Hals-, Nasen- u. Ohrenh. **32**:221 (Nov. 12) 1932.

Hofer reports the case of a child, aged 9 years, with an otogenous pyemia, sinus thrombosis, bulbus thrombosis, a peribulbar abscess and jugular thrombosis, with complete suppuration of the thrombi in the jugular vein; the source of the infection was an old putrefied cholesteatoma. Simultaneously there was a labyrinthine fistula in the horizontal semicircular canal, with injury to the labyrinth but without total loss of labyrinthine function. Cerebral complications which set in about two weeks after an apparently successful intervention on the sinus and bulbus ended in death a few weeks later. At necropsy a large bifurcated abscess was found in the right frontal lobe, and another one in the right occipital lobe, which had perforated into the posterior horn of the lateral ventricle. The age of the abscesses could not be determined. The large ones had a pyogenic membrane; the small

one did not. The author thinks that the abscesses were metastatic, as no direct route for the spread of the infection could be found. The dura of the posterior and median cranial fossa appeared normal. The abscesses of the brain had probably existed for months in latent form, and suddenly became manifest at a time when the sinus and the bulbus thrombosis were in the process of healing. Two days before death 5 cc. of pus was aspirated from the posterior horn of the right lateral ventricle, but the abscess itself could not be reached. No metastases were found in any of the other organs. EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

Diseases of the Skin

A SIMPLIFIED TREATMENT OF RINGWORM OF THE SCALP. IRVING S. BARKSDALE, M. J. & Rec. **136**:494 (Dec. 21) 1932.

The author reports his experiences in a series of eighty cases of tinea trichophytina capitis in which the patients were treated with the following prescription: a bismuth compound of hexamethyl-triamic-triphenylcarbinol chloride, 1 Gm.; salicylic acid, 10 Gm.; 70 per cent alcohol, from 98 to 100 cc. Application of this solution was made daily when possible until healing commenced, which was usually after the seventh to tenth treatment. Four cases are reported in detail.

WILLIAMSON, New Orleans.

HEREDITARY HEMORRHAGIC TELANGIECTASIA WITH A REPORT OF FIVE CASES IN TWO FAMILIES. RALPH C. LARRABEE and DAVID LITTMAN, New England J. Med. **207**:1177 (Dec. 29) 1932.

Five typical cases of hereditary hemorrhagic telangiectasia are reported. They occurred in two families and showed the classic picture: (1) a definite hereditary basis, (2) visible telangiectases, distinctly pathologic in number and distribution and (3) a tendency to bleed from such lesions.

While these cases are usually not recognized until early adult life, the definite history of hemorrhages, particularly from the nose, during childhood should suggest this possibility. The best treatment is probably cauterization of the spots as they occur.

GENGENBACH, Denver.

EXFOLIATING DERMATITIS OF NURSLINGS. G. PAISSEAU, P. TOURANT and G. A. PATEY, Arch. de méd. d. enf. **36**:81 (Feb.) 1933.

In reporting a case of Ritter's disease and in reviewing the literature of this rare disease since the first description by Billard in 1828, the author discusses its etiology, clinical features, evolution, pathology, complications and diagnosis. He concludes that the disorder is a variety of generalized pemphigus attacking exclusively new-born infants and nurslings. Its etiology has not been determined, and, although the disease is probably of infectious origin, its contagiousness is disputed. It is found occasionally in central Europe but is extremely uncommon in France, where only five authentic cases have been reported within a century, two of these being in babies of Polish antecedents, which gives rise to the question of an ethnic influence. Most cases are rapidly fatal.

AMESSE, Denver.

TWENTY-EIGHT CASES OF HYPERKERATOSIS PALMARIS ET PLANTARIS (MAL DE MELEDA) IN THE SAME FAMILY. J. HUTINEL, H. DIRIART and A. G. DREYFUSS, Bull. Soc. de pédiat. de Paris **30**:220 (April 19) 1932.

The authors report twenty-eight cases of hyperkeratosis palmaris et plantaris in five generations of the same family. Twenty-seven members had hyperkeratosis of the palms and the soles, and one member had involvement of the palms only. The sexes were about equally afflicted. The disease was transmitted through the

male and female lines about evenly. It occurred in every generation, but was never observed in the children of parents who were both free from the disease.

BENJAMIN, Montreal, Canada.

THREE CASES OF ACRODYNIA IN CHILDREN. R. A. MARQUÉZY and DENISE ROUGET, Bull. Soc. de pédiat. de Paris **30**:239 (April 19) 1932.

The cases of three patients with acrodynia with marked psychic disturbances are reported. The disease often resembles encephalitis. A neurotropic virus affecting the vegetative nervous system is mentioned as a probable etiologic agent.

BENJAMIN, Montreal, Canada.

INFECTIVITY OF CHILDREN SUFFERING FROM ERYTHEMA NODOSUM. HANS OPITZ, Kinderärztl. Praxis **3**:337 (Aug.) 1932.

Since Walgren's work on the finding of tubercle bacilli in the washings from the stomachs of children with erythema nodosum, Opitz has discovered that in some cases the patients may retain their infectivity over long periods. The clinical symptoms, the roentgen findings and the results of the sedimentation test are not adequate guides to the length of time the infectivity persists. The author advises that children with erythema nodosum should not be allowed to return to school or to mingle with other children until the washings from the stomach show negative findings when injected into guinea-pigs after intervals of two weeks.

HUENEKENS, Minneapolis.

VEGETATIVE NEUROSIS OF EARLY CHILDHOOD (FEER): ACRODYNIA. EMIL FEER, Kinderärztl. Praxis **3**:389 (Sept.) 1932.

Feer lists the chief symptoms of acrodynia: psychic depression; disturbance of sleep; anorexia; prolonged sweating; erythema; itching; sweat-cold cyanotic hands and feet, with desquamation of the skin; decreased motility; rapid pulse; high blood pressure, and trophic disturbances. He emphasizes the importance of the increased blood pressure. Even in the first years of life the systolic pressure may be from 120 to 150 mm. of mercury; the diastolic pressure is also increased. Examination of the blood shows from 6,000,000 to 7,000,000 red blood cells, with from 80 to 90 per cent hemoglobin (Sahli), increased viscosity, and a lowered sedimentation reaction. The relative increase of red blood cells is due in part to loss of fluid from excessive sweating and in part to the direct involvement of the vegetative nervous system.

The pathologico-anatomic findings are the most important in the vegetative nervous system. The conditions found are caused by an unknown toxin or virus; whether the disease is infectious or degenerative is still undecided. The treatment is symptomatic; atropine, calcium and the ultraviolet rays from the mercury vapor arc in quartz are the most effective therapeutic agents. In a recent case striking results were obtained with phenyl-ethyl-hydantoin.

HUENEKENS, Minneapolis.

EARLY TREATMENT OF ANGIOMAS. MARTIN GUMPERT, Kinderärztl. Praxis **3**:397 (Sept.) 1932.

When confronted with a growing hemangioma, it is the duty of the pediatrician to advise early intervention, even in the first few days of life. The choice of treatment depends on the type and location of the lesion and may be carbon dioxide snow, cautery, diathermy or surgical intervention. The author has had insufficient experience with Buckey's roentgen treatment to be able to judge its efficacy. He does not recommend radium because to be effective it must be used in almost toxic doses. In surgical treatment high frequency currents are of value in causing rapid and thorough coagulation of the blood.

HUENEKENS, Minneapolis.

YELLOW PIGMENTATION OF THE SKIN ACCOMPANYING CAROTINEMIA. E. MORO, Acta pædiat. **13**:364 (June 6) 1932.

The pigmentation of the skin that is associated with a diet rich in carotenoids is most easily seen at the rims of the nostrils, on the forehead and the chin and particularly behind the ears and over the knuckles of the fingers and toes. In well marked cases it may be found on the palmar and plantar surfaces and elsewhere, but less commonly. The coloration is probably located in the epidermis and is best revealed where the skin is naturally transparent or can be made so on pressure. The most marked examples are seen in subjects who tend to sweat freely.

McINTOSH, New York.

OCCURRENCE OF TUBERCLE BACILLI IN THE GASTRIC LAVAGE FROM 100 CONSECUTIVE CASES OF ERYTHEMA NODOSUM. J. PHILIPSON, Acta pædiat. **13**:393 (June 6) 1932.

Sixty-six of a hundred cases of erythema nodosum occurred in girls. In four cases the result of the cutaneous test with 10 mg. of tuberculin was negative; the remaining subjects gave positive reactions to tuberculin. The search for tubercle bacilli was made at the time of the eruption or soon after its onset; in forty-seven of ninety-six cases the organisms were recovered. In patients with a relatively mild degree of involvement of the hilar nodes as shown by roentgenograms, the number of recoveries of organisms was somewhat increased by repetition of the lavage of the stomach on two successive mornings. Tubercle bacilli remained demonstrable in the sputum by gastric lavage from two to six months after tuberculous erythema nodosum had disappeared.

McINTOSH, New York.

Surgery and Orthopedics

UMBILICAL HERNIA: TYPES AND TREATMENT. R. FRANKLIN CARTER, Arch. Pediat. **49**:622 (Sept.) 1932.

The writer discusses umbilical hernia from the point of view of types, symptoms, diagnosis, prognosis and treatment.

WADDELL, University, Va.

SURGICAL ASPECTS OF PERICARDITIS. E. D. CHURCHILL, New England J. Med. **208**:774 (April 13) 1933.

To the surgeon the syndrome of cardiac tamponade is of utmost importance. The signs of tamponade are venous engorgement, reduced arterial pressure, engorgement of the liver and peripheral edema.

In tapping the pericardium, the author prefers to enter the chest between the seventh costal cartilage and the xiphoid cartilage, with the needle directed upward and backward. In acute suppurative pericarditis, surgical intervention, preferably with open drainage, is indicated.

Relief is sometimes obtained in the constrictive type of chronic adhesive pericarditis, the so-called Pick's syndrome. Of thirty-seven cases found by the author in the literature, the operation was not completed in five. There were seven operative deaths, two patients showed no improvement, and in nineteen cases there were good results.

GENGENBACH, Denver.

OSTEOGENIC SARCOMA. HUGH JETER, South. M. J. **26**:268 (March) 1933.

The authors report fifteen cases of osteogenic sarcoma. Osteogenic sarcoma is a tumor of the adolescent, occurring at the age of development of the metaphysis, the predominating site of the tumor. In each of the fifteen cases reported, the tumor occurred at the end of a long bone and was apparently of metaphyseal origin. In thirteen of the fifteen cases there were pulmonary metastases; in twelve cases amputation had followed high voltage roentgenotherapy. Twelve of the fifteen

patients are dead. There seems to be a mortality rate of about 100 per cent regardless of treatment. The average duration of life from the onset of illness to the time of death in the twelve cases was twelve months. SCHLUTZ, Chicago.

THE EARLY TREATMENT OF CONGENITAL TALIPES. N. D. ROYLE, M. J. Australia **2**:803 (Dec. 31) 1932.

Royle stated that in the treatment of congenital talipes equinovarus the varus should be dealt with first. Corrective passive movements should be performed daily and the improved position maintained by the use of molded plaster of paris splints, new splints being made every few days. By this method it is possible to correct the varus deformity in from two to three weeks. Following this the treatment of the equinus should be commenced and continued until the dorsum of the foot approaches the anterior surface of the leg and until the child has been walking for several months. Dorsiflexion is accomplished by means of a thin strip of wood applied to the sole of the foot, with straps connecting the foot and knee and the buckles. GONCE, Madison, Wis.

LARGE VESICAL CALCULUS IN A GIRL SIX YEARS OLD. M. LESNE and GUILLAIN, Bull. Soc. de pédiat. de Paris **30**:277 (April) 1932.

A vesical calculus, about the size of a small hen's egg and weighing 18 Gm., was removed from a 6 year old girl by means of suprapubic cystotomy. The center of the calculus was composed of calcium urate, and this was surrounded by calcium carbonate and calcium phosphate. As a rule, there is a long period without any marked urinary symptoms, and this probably accounts for the large size which vesical calculi usually attain in children. The right lower extremity was 2 cm. shorter than the left and was externally rotated. This was caused by osteomyelitis of the head of the right femur when the child was 3 years old. A roentgenogram showed almost complete atrophy of the head of the bone, which had subluxated posteriorly and laterally and had created a new socket in the ilium with which it articulated. BENJAMIN, Montreal, Canada.

PYLORIC STENOSIS IN INFANCY. O. WIEDHOPF and H. BRÜHL, Deutsche Ztschr. f. Chir. **238**:653, 1933.

The authors studied 50 cases occurring between 1925 and 1932. There was no distinct seasonal incidence; 84 per cent of cases were in males; nothing new is suggested with respect to the etiology. Medical treatment was employed in thirty-five cases of all degrees of severity, in which all of the patients recovered except two. In both cases death occurred two or three weeks after vomiting had ceased; in one case death was caused by pyelonephritis, and in the other by grip. The principles of the medical treatment were: removal from the breast, because the act of nursing stimulates an increase in tone of the pyloric musculature and also increases the tendency to vomit; catheter feeding for the same reason; the use of small amounts of breast milk to which, in some cases, carbohydrate was added; gastric lavage; parenteral administration of dextrose in Ringer's solution; intramuscular or intravenous administration of blood, and, most essential of all, individual nursing care.

Two of fifteen patients who were operated on died; all of them were males. One patient had an exudate in the abdominal cavity at the time of operation and died of peritonitis ten days later; the other infant died of postoperative hemorrhage.

Infants in whom there is such marked loss of weight that life is considered in immediate danger should be operated on without delay. When the vomiting appears relatively late and the loss of weight is not marked, medical measures should be given a trial. Cases occupying a middle ground must be judged individually.

Experiments on animals indicated that hunger and loss of weight may be accompanied by injury to the intestinal and pancreatic ferments, especially to lipase and trypsin. This may explain the slow recovery in some cases after cessation of vomiting. Early operation tends to avoid this. Long continued pyloric obstruction causes dilatation of the stomach and delayed emptying time. After operation, the stomach usually returns to a normal configuration in ten days. One patient treated medically died a year later of pulmonary tuberculosis. At necropsy the stomach was found to be still greatly dilated. In other patients treated medically roentgen study indicated gastric atony, gastric dilatation and ptosis and occasionally, from two to five years later, delayed emptying time. Such findings were never observed in cases in which operative procedure had been followed.

Only the Rammstedt operation was used. Ether anesthesia was preferred. Emphasis is placed on delivery through the incision only of the part to be operated on. Sharp dissection should be used only for the initial incision of the pyloric tumor; the operation is completed by blunt dissection, which favors hemostasis. In spite of every care, the most experienced operator occasionally pierces the mucous membrane. If this is noticed, however, the opening can be closed without complications. Postoperative care is of the greatest importance; several cases are reported which illustrate this in detail. The average postoperative stay in the hospital was from eleven to seventeen days.

GLASER, Rochester, N. Y.

TREATMENT OF EMPYEMA IN CHILDHOOD WITH SODIUM TAUROCHOLATE. EUGENIO SCHWARZ, Kinderärztl. Praxis **3**:542 (Dec.) 1932.

The method of treatment with sodium taurocholate was originated by Cocchi, of Florence, and is effective in pneumococcic empyema. Every two or three days the author aspirates as much pus as possible from the pleural cavity and by means of a three way stopcock injects a 5 per cent solution of sodium taurocholate, never using in a single dose more than 2 Gm. for an infant under 1 year of age, or more than 4 Gm. for older children. In thirty cases the mortality was 26 per cent; for infants under 1 year of age, it was 50 per cent. While the results are admittedly not brilliant, the method has a place in cases in which surgical intervention is contraindicated.

HUENEKENS, Minneapolis.

OSTEOMYELITIS OF THE UPPER JAW IN THREE INFANTS. W. HERZAU, Klin. Monatsbl. f. Augenh. **90**:55 (Jan.) 1933.

The author states that until recently the subject of osteomyelitis of the upper jaw in infants has not been found much in ophthalmic literature. He mentions the articles of D. Bosse and Remky. He thinks that in the majority of the cases the ocular symptoms dominate the picture, and that the disease is so rare and the signs so varied as to cause difficulty, leading to errors in the proper operative handling which make the prognosis unfavorable.

He mentions the possible etiologic factors, namely, an infection in the alveolar border, especially caused by mastitis in the mother, and the rhinologic cause.

The clinical picture shows severe swelling, chemosis, exophthalmos with limitation of motion and fistula, mostly in the infra-orbital margin, in the corner of the eye, in the hard palate, in the alveolar process and, in rare cases, in the nose. The disease is to be differentiated from phlegmon of the tear sac chiefly by its site. The swelling, as a rule, is more severe in the eyelid than over the tear sac. In many cases it is most difficult to differentiate the condition from orbital phlegmon; nevertheless, it can be recognized from the site of the fistula, the lack of swelling of the upper jaw and the purulent secretion in the nose.

Frequently there results metastatic suppuration in other bones and organs, as for example in the brain and lungs, so that a mortality of 29 per cent is not to be wondered at. As an ocular complication optic atrophy has been described.

The therapy consists in the widest possible removal of the infected region through an operative opening, which, for cosmetic reasons, should be done from within when possible.

The author reports three cases.

The first case occurred in a child, 6 months old, presenting typical symptoms. An incision into the lower orbital margin disclosed pus, but recovery followed only after radical removal of the tooth bud by the rhinologist.

The second case was that of a child, 4 weeks old, who for two weeks had had redness and swelling of the right lower lid which had been treated by an ophthalmologist as a phlegmon of the tear sac. This case presented typical symptoms with high fever. An incision in the lower lid yielded foul-smelling pus. Besides this there was bilateral otitis media. With the child under ether anesthesia, the rhinologist made an incision in the upper jaw. Two free sequestrums and a tooth bud were removed. Soon a fistula appeared in the lower orbital margin; later this was incised and a further sequestrum removed. Recovery ensued.

The third case was that of a child, 6 weeks old, who had been sick for a week. The upper lid was swollen, with induration of the lower lid, especially in the region of the tear sac. In the conjunctival sac there was pus. The eyeball was protruded without chemosis or any other abnormal findings. The upper jaw was swollen on the right side, and a purulent secretion was found in the nose. Under ether anesthesia, an incision was made through the face over the upper jaw, and considerable pus was evacuated along with a tooth bud. Recovery with optic atrophy resulted.

In discussing the cases the author stated that the external incision in two children resulted in no cosmetic defects. Whether the removal of the tooth bud can lead to a deformity of the upper jaw as a result of the decreased development on the diseased side only the future can show. In the first child several years later there was no deformity. VAIL, Cincinnati. [ARCH. OTOLARYNG.]

PECULIARITIES OF OSTEOMYELITIS IN EARLY CHILDHOOD. GUNTHER BASCHLAU, Monatschr. f. Kinderh. **55**:280 (Jan.) 1933.

A complete and interesting study is given of forty-two cases of osteomyelitis in the Finkelstein clinic. The characteristic of this disease in nurslings is its tendency to localize in the epiphyses. From here, the disease rapidly spreads to involve the joints, although one in three or four cases may lead to metastases. The disease is always much more acute in children than in adults. Seldom does one see the chronic fistula and elimination of sequestrums. The clinical course varies from mild cases to those of the severe, septic, toxic type. The mortality rate is reported as about 66 per cent, but with the treatment advocated twenty-six of the forty-two patients at the clinic were saved.

The article describes unusual locations of infection, such as the skull, and the upper and lower jaws, with case reports.

The treatment is preeminently conservative. One should never be too hasty, but should wait until the abscess is completely formed, and then open it without disturbing the bone. Even when the joint is involved, better results are obtained by aspiration repeated several times. Even purulent joints of small children have a great tendency to heal without functional disturbance, if one does not injure the synovia with hard drains. Again in this procedure, great conservatism must be employed, and the phlegmon opened without opening the joint.

GERSTLEY, Chicago.

GENERAL SYMPTOMS ASSOCIATED WITH THE SURGICAL TREATMENT OF PYLORIC STENOSIS. W. MUNTING, Monatschr. f. Kinderh. **55**:341 (Jan.) 1933.

In a series of fifty operations for pyloric stenosis, the writer reported a continuance of vomiting for several days in 70 per cent. Eighty-two per cent of the patients showed fever. Symptoms of marked dehydration developed in several, and death occurred in six following definite nutritional disturbance. Convulsions developed in two children.

The mortality rate was 12 per cent. The writer explains the mortality and these symptoms as being due to the desperate nature of the cases. In none of them had operation been performed except as a last resort.

GERSTLEY, Chicago.

PROGNOSTIC VALUE OF INTRAPLEURAL INJECTIONS OF DEXTROSE IN EMPYEMA. DOSKOCIL and PROCHASKA, Časop. lék. česk. **70**:1738 (Dec. 18) 1931.

In benign cases of empyema repeated injections of 20 cc. of 10 per cent dextrose into the pleural cavity after aspiration of pus changed the reaction from alkaline to acid and inhibited the growth of pneumococci. The exudate became thicker, and dextrose was demonstrable in from twenty-four to forty-eight hours after its injection. In other cases acidification followed rapidly but recovery took place, and the presence of dextrose was demonstrated only after from fifteen to twenty injections. In the third group neither change in reaction nor demonstration of dextrose followed the injections; recovery resulted in only one case, and that was only after retraction of the thoracic wall. Increased acidity of the exudate and demonstration of dextrose within forty-eight hours after its injection can be used as a favorable prognostic point.

STULIK, Chicago.

SURGICAL THERAPEUSIS OF PERICARDITIS WITH EFFUSION. JAN KRIZAN, Časop. lék. česk. **70**:1740 (Dec. 18) 1931.

The author reviews the literature and presents a classification of pericarditides. A description of various operative procedures is given. These include the posterior or left scapular line methods. The author removed 1,560 cc. of fluid in eight fractions over a period of fourteen days by the Curschman method, i. e., making the incision in the left mammary line in the fifth to seventh interspace. Lavage with 200 cc. of 5 per cent ethylhydrocupreine left a residuum of 6 cc. Recovery resulted.

STULIK, Chicago.

DOES ACUTE APPENDICITIS IN GIRLS OR YOUNG WOMEN RESULT IN STERILITY? P. BULL, Norsk mag. f. lægevidensk. **93**:1285, 1932.

The author comes to the conclusion that acute appendicitis in girls or young women may result in sterility in some instances. This is particularly true in cases in which severe attacks have been treated medically or in which the operation has been performed late in the attack. On the other hand, it must be said that even in cases in which the appendicitis has produced marked changes in the pelvic organs a normal pregnancy may occur.

TAVERUD, Oslo, Norway.

Miscellaneous

THE PROBLEM OF DENTAL CARIES. THEODORE ROSEBURY, Arch. Path. **15**:260 (Feb.) 1933.

The author discusses the clinical and pathologic aspects of dental caries. He also cites a vast amount of data obtained by experimentation, and critically analyzes the numerous theories concerning the etiology of dental caries. The present knowledge in reference to the subject is well summarized.

LEMASTER, Evanston, Ill.

BROMID INTOXICATION. CHARLES W. WAINWRIGHT, Internat. Clin. **1**:78 (March) 1933.

The bromide ion acts chiefly on the central nervous system. Motor areas show decreased irritability and retardation in response to stimulation. The intellectual and psychic centers are depressed as well. The symptoms of intoxication consist in the appearance of acne-like lesions of the skin, restlessness, tremor of the hands,

tongue or face, ataxia, slurred and indistinct speech, pupillary changes, variable changes of the deep reflexes, muscular weakness, hallucinations, delirium, disorientation and loss of memory. Treatment consists in withdrawal of the drug and the giving of sodium chloride, which accelerates the elimination of the bromide ion from the body.

MILLER, South Bend, Ind.

CLINICAL EXPERIENCES WITH SYNTHETIC EPHEDRINE. HARRY A. KERN and HARRY P. SCHENCK, J. Allergy **4**:9 (Nov.) 1932.

A comparison of the therapeutic effect of natural and synthetic ephedrine on 260 patients suffering from asthma, either infectious or allergic, hay fever or vasomotor rhinitis was made. Both drugs were given to 100 patients at different times, the natural drug to 100 and the synthetic to 60. The dose was 25 mg. given orally three times a day. In the palliative treatment of these diseases, the synthetic ephedrine was as efficacious as the natural drug. The effect of the synthetic preparation on the blood pressure was less than that of the natural preparation. Unfavorable effects were produced with the synthetic drug in 9 per cent of the patients as compared with 23 per cent with the natural drug. Hypersensitiveness to both drugs has been observed.

At present there is no economy in the use of the synthetic preparation. Increased use of it may reduce the price.

HOYER, Cincinnati.

PHYSICAL MEASUREMENTS OF ADOLESCENT SCHOOL BOYS IN RELATION TO SCHOLASTIC ATTAINMENT AND PROWESS IN GAMES AND SPORTS. ALFRED A. MUMFORD, J. Hyg. **33**:80 (Jan.) 1933.

This is the continuation of a detailed study over a period of ten years, other reports having previously appeared in the *Journal of Hygiene*. It is believed that a relationship exists between physical measurements and physical and mental ability and aptitudes which may be of value in the proper selection of a program for a given child. It may also explain many failures.

The height, weight, chest girth and vital capacity were taken for 797 boys. Comparisons with their scholastic and athletic ability were made. Those who won colors at games or credits at sports appeared to have attained a greater growth at each age than those who did not. Increased growth at a given age was associated with more advanced scholarship. The differences were small but uniform with few exceptions. The same conclusions were reached concerning vital capacity. Ample chest girth with ample oxygen reserve is important in determining ability. At the age of 17, when adolescence is completed, the differences are less than for the preceding years.

Physical growth in relation to prowess in individual games or sports also was noted, indicating, for instance, that sprinters, Rugby players and swimmers are relatively tall and heavy, while gymnasts and long distance runners are relatively short and light.

JANNEY, Milwaukee.

THE PEDIATRICIAN AND PUBLIC HEALTH. CLIFFORD G. GRULEE, J. Pediat. **2**: 265 (March) 1933.

Fundamental problems facing the pediatrician and the public health official are discussed. Responsibility must rest on the public health authorities for such general measures as inspection of food, regulation of milk and analysis of water, which constitute protective measures that can be applied in a mass. On the other hand, the physician must care for his private patients when they are sick and manage those procedures which necessarily involve a direct relationship with the patient. Throughout infancy, individual attention is required. In children of school age the usual method is to have examinations for physical defects conducted by the school physicians, following which the children are referred to their private physicians and dentists for treatment. School children should receive adequate instruction in personal and public hygiene. Much can be accomplished by educating the masses of people concerning preventive medical measures.

LEMASTER, Evanston, Ill.

STUDIES OF MORPHINE, CODEINE AND THEIR DERIVATIVES. NATHAN B. EDDY, J. Pharmacol. & Exper. Therap. **45**:339 and 361 (July) 1932.

From funds furnished by the Bureau of Social Hygiene, the National Research Council has undertaken a study of addiction to drugs. The pharmacologic aspects of this question are being carried on by the author at the pharmacologic laboratory of the University of Michigan, and are to be reported from time to time in the *Journal of Pharmacology and Experimental Therapeutics.*

The first paper presents the methods and the second paper the results with certain derivatives of codeine which seem to have definite advantages (in animals) over codeine itself. The papers are not sufficiently complete for fuller abstraction. Other papers are promised.

PILCHER, Cleveland.

REPORT OF TWO HUNDRED AND EIGHTEEN COMPLETED CASES SEEN AT THE WESTCHESTER COUNTY PRENATAL CLINIC IN 1931. MATTHIAS NICOLL, JR., and EDWARD H. MARSH, New York State J. Med. **32**:1180 (Oct. 15) 1932.

In the Westchester County Clinic, 5.5 per cent of the patients were found to be syphilitic. Syphilis was more common among the colored patients—15.5 per cent.

The fetal and infant mortality was high, over 10 per cent of the potential lives. This high mortality is obtained because the clientele of the clinic consists of many who normally contribute most to fetal and to infant mortality.

AIKMAN, Rochester, N. Y.

THE CONTRIBUTION OF PEDIATRICS TO DENTAL HEALTH. ROYAL STORRS HAYNES, New York State J. Med. **32**:1234 (Nov. 1) 1932.

Ninety-five per cent of the 45,000,000 children of this country are said to have dental caries, and 85 per cent, defects of occlusion. The child with dental caries has imperfect nutrition. The pediatrician knows that positive harm may result from poor teeth, and his work in nutrition should make it possible to prevent much of this dental trouble.

AIKMAN, Rochester, N. Y.

RELATION OF DISEASES OF THE MOUTH TO PEDIATRICS. LEROY MINER, New York State J. Med. **32**:1237 (Nov. 1) 1932.

The cells of the first deciduous teeth are laid down about the ninth week of fetal life, and those of the first permanent molars at the seventeenth week. For the first two years of life active calcification is progressive. Prenatal clinics and those for small infants must cooperate with the dentist if the proper development of teeth is to be secured. The effects of general disease and deficient diets on the growth of teeth are stressed.

Decayed temporary teeth may cause much trouble, fretfulness, irritability and disturbances of the gastro-intestinal tract. Infections in other parts of the body may also develop.

AIKMAN, Rochester, N. Y.

RELATION OF DISEASES OF THE MOUTH AND TEETH TO PEDIATRICS AND INTERNAL MEDICINE. WILLIAM D. TRACY, New York State J. Med. **32**:1239 (Nov. 1) 1932.

Teething usually causes no symptoms, but irritation, inflammation due to pressure and swelling may be marked, and may produce symptoms. In certain cases difficult dentition assumes a real and sometimes a serious aspect. The child's teeth should be examined by a dentist at 2½ or 3 years of age and every six months thereafter.

Dental caries is a serious matter and is the most prevalent and widespread of all human diseases. Every effort should be made to protect the deciduous teeth. The death of pulp in the mouths of adolescent patients, formerly considered lightly, "is now regarded as nothing short of a tragedy." The causes and prevention

of dental caries are still unsolved problems. The dietetic approach is now dominant. If this enigma is to be solved, the dental profession must have the assistance of physicians.

AIKMAN, Rochester, N. Y.

CAUSES OF ILLNESS IN 9,000 FAMILIES, BASED ON NATION-WIDE PERIODIC CANVASSES, 1928-1931. SELWYN D. COLLINS, Pub. Health Rep. **48**:283 (March 24) 1933.

This is the most comprehensive study of its kind ever attempted. Although data on mortality are now available for all except 1 state, records on sickness have heretofore been meager. A total of 8,758 white families in 130 localities in 18 states was observed for illness for a period of twelve consecutive months, between February, 1928, and June, 1931. An illness rate of 850 per thousand persons was found. Illnesses that caused loss of time from work or from school amounted to 516 per thousand persons. Illnesses during which the patient was confined to bed for one or more days amounted to 434 per thousand population. Colds and bronchitis were by far more common than any other illnesses. The next most frequent illnesses included influenza and grip, accidental injuries, tonsillitis and laryngitis, conditions of the stomach, measles and pregnancy.

LEMASTER, Evanston, Ill.

THE PHYSICIAN AND THE WEST VIRGINIA WHITE HOUSE CONFERENCE. GEORGE M. LYON, West Virginia M. J. **29**:175 (April) 1933.

This article is a discussion of the plans of the West Virginia White House Conference on Child Health and Protection and the many problems to be surveyed and studied. An appeal is made for the unselfish wholehearted cooperation of both lay and professional persons, and of professional, official and lay organizations in order that the surveys and studies may be complete and far-reaching in the correction of existing evils and in creating new programs along needed lines.

SHAWKEY, Charleston, W. Va.

TRANSFUSION OF BLOOD IN INFANTS. HUBER and ABRICOSSOFF, Nourrisson **20**:341 (Nov.) 1932.

This article is a plea for more transfusions for sick and dehydrated infants. The authors prefer the use of citrated blood; they inject it directly into the longitudinal sinus, as first recommended by Marfan in 1898, or into one of the superficial veins. Matching of blood in infants under 6 months of age is not necessary. Intraperitoneal transfusions are condemned as being too dangerous.

MCCLELLAND, Cleveland.

WEIGHT CURVES OF BABIES OF OLDER WOMEN. M. GAYTA, Prat. pediat. **10**:489 (Nov.) 1932.

These studies deal with patients seen in the "Borgo Dora" dispensary in Turin during the past twenty-five years, and include the babies of 251 women who ranged between 35 and 48 years of age. The author arbitrarily chooses a parabolic weight curve increasing from 3,100 Gm. at birth to 9,000 Gm. at 1 year of age, and terms it the "regular" curve. About 55 per cent of the babies of mothers under 35 years of age showed regular curves, whereas only 34 per cent of those of mothers over 35 years grew regularly. The tables indicate that babies fed artificially develop at nearly the same rate, no matter what the age of the mothers, while the breast-fed babies of younger mothers and those given mixed feedings develop better than the babies of mothers over 35 years who are fed similarly. Nearly twice as many babies of elderly primiparas had regular curves when they were given supplementary feedings than when they were breast fed alone.

Dr. Gayta presents the following table of the average weights at birth in Italian clinics during the past century:

Year	Gm.	City
1844	3375	Milan
1880	3250	Pisa
1882	3230	Turin
1882	3200	Modena
1890	3175	Milan
1901	3175	Pisa
1903	3060	Ferrara
1912	3060	Turin

DOOLEY, Kent, Conn.

MODERN CONCEPTION OF SOCIAL SERVICE. GREGORIO ARÁOZ ALFARO, Bol. Inst. internac. am. de protec. a la infancia **6**:221, 1933.

The author presents the modern conception of social service and recalls the definitions made by Drs. Pierre Joannon, Paulina Taruggi and Alice Masarykova at the First International Conference of Social Service in Paris in 1928, and the words of Rev. D. H. Le Blond, at the Sixth Pan-American Child Congress in Lima in 1930. He refers to opinions expressed in the monograph of the School of Social Service of Santiago, Chile, and quotes other opinions, in order to stress the difference between social service and charity, even though the two are not antagonistic. The author emphasizes the latter point because he has noticed in some churches a certain hostility toward social visitors, in spite of the fact that social service has spread widely in such Catholic countries as France, Austria and Belgium.

In analyzing the work of a good social visitor, one can assume that she must possess a knowledge of medicine, hygiene and legislation, as well as information in regard to public and private institutions. Good will and self-denial are not sufficient; special capacities and an adequate technical training are also necessary.

In addition to temporary relief, preventive measures should be carried out. A characteristic goal of modern social service is the reconstruction and consolidation of the family, so as to enable each member to sustain himself by his own efforts.

AUTHOR'S SUMMARY.

SOCIAL SERVICE IN THE INSTITUTE OF MATERNITY OF THE BENEVOLENT SOCIETY OF BUENOS AIRES. ALBERTO PERALTA RAMOS, Bol. Inst. internac. am. de protec. a la infancia **6**:244, 1933.

The Institute of Maternity of the Benevolent Society of Buenos Aires has the following sections: a common hospital, in which prospective mothers may rest during the last months of pregnancy; a maternal hospital to shelter mothers with their new-born infants; an infants hospital for children with or without their mothers; a hospital for the care and cure of sick pregnant women; an obstetric section, which mothers enter at the time when labor begins; an isolation section for contagious cases; a gynecological section for the care of sick women; external clinics for prenatal care and gynecology and a clinic for the care of infants, with a Goutte-de-lait. Dental, ear and nose and prenuptial services are annexed to the external clinics.

The social service department of the Institute of Maternity, which was started more than four years ago, has the following aims: to make it possible for prospective mothers to end their confinement under the best physical and moral conditions, and to make it possible for mothers to keep their children, promoting breast-feeding. All women seeking the aid of the Institute for the first time must be examined at the office of the social service department, where the visitors start a record sheet which they complete with data obtained during visits they pay at the homes, with that available at the external clinics or at the internal maternity clinic, and with that obtained by them in carrying out their medical and economic and social duties.

The activity of the social visitors is evidenced in the statistical records covering the period from July 1, 1928, to Sept. 15, 1932. During this period 13,561 women and 4,457 children, making a total of 18,018 cases, attended the external clinics of the social service department; 1,470 cases were followed up, and 990 were dismissed; 1,817 calls were made at the homes; 897 letters were written; 632 commissions and 36 legal consultations were carried out; 40 marriage licenses were obtained from the civil justice; 701 children were placed with their mothers, and 303 children were placed elsewhere; in 276 cases cooperation was sought from other hospital services, and in 324, from other social service centers; in 947 cases cooperation was established between different services of the Institute; 624 pregnant women were sent to the pathologic and observation sections of the Institute, and 250 calls were made at the request of the clinic for prophylaxis. The aid given amounted to $2,201.40 in cash, in addition to clothes, shoes and the like. The number of outside confinements was 71. Sixty-seven marriages, 94 legitimations, 784 cases of prevention of abandonment, 301 legal recognitions and 52 reconciliations were the moral returns of the social service departments.

AUTHOR'S SUMMARY.

CONTRIBUTION OF SCHOOL EXCURSIONS TO EDUCATION. PEDRO GARGIA VALDÉS, Bol. Inst. internac. am. de protec. a la infancia **6**:268, 1933.

The author makes a study of school excursions from a historical and a psychopedagogic point of view. He points out some aspects of the subject which are well known to all teachers but which are usually neglected in practice. The teacher's direction is required to teach observation of what would otherwise pass unnoticed by the pupils; if this direction fails, the excursion becomes a mere walk and loses a great part of its educational value. The teacher should visit beforehand the site of the excursion, so as to study it carefully and be prepared to answer the innumerable questions that the children may ask if they are left at liberty to express their investigating spirit. The pupils should demonstrate what they have learned by making summaries, drawings, maps and charts, collecting the different objects they have found, exchanging others with the children of the places visited and corresponding afterward with the latter. Another important item is to make the excursions systematic; they should not be made without a plan or at random.

The author, who is the superintendent of schools in the province of Pinar del Rio, Cuba, organized 1,162 excursions during the school year of 1930-1931, and 1,319 during that of 1931-1932. In order to make the trips more interesting, city children were taken to the country, those from the plains were taken to the mountains, those living inland were taken to the seashore, and vice versa. Interest was also aroused in organizing a basket-ball contest in which school children from every locality played a part, the final meeting taking place at the capital.

AUTHOR'S SUMMARY.

PRACTICAL TEACHING OF CHILD CARE TO FUTURE TEACHERS. EUGENIA S. YANNUZZI, Bol. Inst. internac. am. de protec. a la infancia **6**:286, 1933.

The author stresses the importance that the teaching of child care has acquired in Uruguay and in the normal school for women in particular, where the practical phase of the subject is taught. The teaching is carried out at the Institute of Pediatrics and Puericulture under the direction of Prof. Luis Morquio, who gives weekly lessons during the year to normal school students and to the mothers who attend the clinic with their babies, where he examines each child. The students are trained in the care of children, the bathing of babies, in dressing them with clothes they themselves have made and in preparing their food when necessary.

AUTHOR'S SUMMARY.

Society Transactions

NORTH PACIFIC PEDIATRIC SOCIETY

Portland, Ore., July 29, 1933

H. E. Coe, M.D., *in the Chair*

"Fits" Resulting from a Fall. Presented by Dr. Harold K. Faber, San Francisco.

A girl, 9 years old, was admitted to the hospital with a complaint of "fits." The patient fell 12 feet when she was 4 years of age, but there were no signs of intracranial injury at that time. A month later she was indisposed and drowsy for three weeks. In 1929 she began to have spells, with nodding of the head, particularly at meal times. The number of attacks varied from six to thirty a day. They increased in severity until toxic and clonic spasms set in, and the left side became spastic. The physical and neurologic examinations gave negative results. Encephalograms showed a large collection of air over the right side of the cortex, which was interpreted as the sequel to a cerebral hemorrhage resulting from the fall. No therapy was indicated at this time.

DISCUSSION

Dr. L. H. Smith, Portland, Ore.: I question the absence of neurologic disturbances explained by the fact that the damage was too far back.

Dr. H. E. Coe, Seattle: I am interested in the fact that there was no air in the ventricles. This circumstance is probably accidental.

Tertian Malaria. Presented by Dr. Harold K. Faber, San Francisco.

A boy, 3 years old, was admitted to the hospital in October, 1932, with a complaint of chills and fever. The attacks occurred on alternate days, in the afternoon, and on the intervening days the patient complained of being tired. The physical examination gave negative results except for a slightly large spleen and liver. Tests of the blood showed: hemoglobin, 68 per cent; red cells, 3,600,000, and white cells 5,650. The organisms that cause tertian malaria were found in the red blood cells. Treatment with quinine resulted in relief until June, 1933, when there was either a recurrence or a recrudescence. The infection occurred in the hop fields of southern Oregon. Other members of the family also had malaria.

Pelvirectal Achalasia (Hirschsprung's Disease). Presented by Dr. W. H. Bueermann, Portland, Ore.

A boy, 2 years of age, was admitted to the hospital on May 9, severely constipated. He had never had spontaneous stools. The physical examination and laboratory findings were negative. A roentgenogram showed a markedly dilated large bowel. The patient was observed from May 13 to 16, during which time, in spite of enemas, fecal matter accumulated. An enema of one-half hydrogen dioxide and one-half water dislodged a quantity of this material. At operation the left half of the colon was dilated, with no striation or pouching; the right half was dilated, but was striated and pouched. A left sympathectomy, as described by Adson, was performed, including the second, third and fourth ganglions. Several anomalies were encountered. From that time on the stools were spontaneous. As shown anatomically by roentgenograms, the condition was not cured, although the abdomen was much smaller.

DISCUSSION

DR. H. E. COE, Seattle: Since this is a physiologic surgical procedure, the anatomic result is relatively unimportant.

DR. E. J. BARNETT, Spokane, Wash.: I suggest that spinal anesthesia be given a trial in this type of surgical procedure.

DR. L. H. SMITH, Portland, Ore.: I find that mothers whose children are mildly constipated are gratified to know that this patient went for fourteen days without a stool and was unharmed.

ACHONDROPLASIA. Presented by DR. HAROLD K. FABER, San Francisco.

A boy, 2 years of age, was admitted to the hospital with a complaint of difficult breathing and aural trouble. The patient was born with a large head, which was a family characteristic. His developmental history was normal. The physical examination showed obstructed breathing, with the nose depressed. The nasopharynx was short, and the tonsils were prominent. The circumference of the head was 52 cm.; the neck was very short; the humeri and femurs were also short. The fingers were stubby, tridentate and symmetrical. There was marked lordosis of the lower part of the sacrum, and the legs were bowed. A roentgenogram of the skull showed that the distance from the foramen magnum to the glabella was short and that the cortex was dense. The condition had been diagnosed as achondroplasia.

HEMOPHILIA. Presented by DR. HAROLD K. FABER, San Francisco.

A girl, 4½ years old, of Italian parentage, bruised easily. She was admitted to the hospital in June with a history of bruises for two months. There was no nosebleed or other symptoms. The physical examination gave negative results, except for small petechial hemorrhagic spots widely scattered over the body. There was no jaundice or vomiting, and no blood was evident in the urine. The family history was irrelevant. The spleen was palpable. The temperature and pulse were normal. The blood count showed hemoglobin, 82 per cent; red cells, 3,970,000; white cells, 11,350; neutrophils, 56 per cent; eosinophils, 2 per cent; small mononuclears, 42 per cent; platelets, 106,000. The fragility test showed complete hemolysis in from 3.6 to 2.8 per cent of sodium chloride. The bleeding time was from six to twenty-eight minutes; the coagulation time, seven minutes. A transfusion of blood gave temporary relief. The tourniquet test was positive, and the blood platelets increased to 200,000. The conclusion was that we were not dealing with an infectious process. The prognosis varies with a tendency to recurrence. A splenectomy is not indicated unless the symptoms become much worse.

DISCUSSION

DR. F. E. OSGOOD, Portland, Ore.: The differential diagnosis of the condition should be discussed in detail.

DR. R. S. FISHER, Spokane, Wash.: In a case of hemophilia that I saw the bleeding time was temporarily reduced by the administration of ovarian extract, 80 grains (4.6 Gm.) daily.

DR. A. H. SPOHN, Vancouver, B. C.: In a case reported at the last meeting there had been hemorrhage into the spinal canal. The blood platelet count became normal, and the patient has been well since a splenectomy was done.

DR. J. T. ABRAHAM, Wenatchee, Wash.: I should like to ask about the use of antivenom in the treatment of purpura.

POLIOMYELITES. Presented by DR. HAROLD K. FABER, San Francisco.

Poliomyelitis is essentially a generalized infection which becomes secondarily neurologic. Monkeys are not infected unless the virus is applied to the nasal

mucosa or directly to the central nervous system. The virus is exceedingly small, possessing the ability to get into the nerve cells and nuclei. The olfactory nerve cell in the infant's nose is more accessible to the virus; therefore the virus was applied experimentally to the mucous membrane previously treated with dilute hydrochloric acid (p_H 5) and the nerve process dissected out on successive days. The pathologic process was found to be progressing along the nerve tract from day to day. The cell count and pressure of the spinal fluid increased rather early, although a pause was noted between the onset of the symptoms and the paralysis. The disease may become abortive in any stage. Treatment was given to introduce immune bodies in the spinal fluid to prevent passage from one nerve cell to the other. Aycock attempted to prove that treated persons had less extensive paralysis than those untreated. The serum of the donor should be tested for antibodies before it is administered. Intravenous injection is much preferred to the intrathecal method. There is some promise from prophylactic injection for a period of a few weeks.

DISCUSSION

DR. J. B. BILDERBACK, Portland, Ore.: What amount of serum was given?

DR. HAROLD K. FABER, San Francisco: Five hundred cubic centimeters of blood by transfusion.

DR. J. T. ABRAHAM, Wenatchee, Wash.: What percentage of titer was used?

DR. HAROLD K. FABER, San Francisco: From 20 to 70 per cent was the average amount used.

DR. N. W. CLEIN, Seattle: What about the theory of geographic distribution of poliomyelitis?

DR. HAROLD K. FABER, San Francisco: I do not think that carriers account for the spread, although dust might be a factor in distribution.

DR. J. W. ROSENFELD, Portland, Ore.: Why do some children have so much fever and pain while others have none?

DR. HAROLD K. FABER, San Francisco: The amount of fever and pain depends on the amount of involvement of the sensory nerve cells.

DR. H. H. SKINNER, Yakima, Wash.: Why is there such a high percentage of immunity? After from 12 to 14 years of age many children have had only abortive attacks.

DR. N. W. CLEIN, Seattle: Have tests of the skin ever been made with the emulsion?

DR. HAROLD K. FABER, San Francisco: No.

DR. C. U. MOORE, Portland, Ore.: Might not the application of various nasal remedies increase the susceptibility to the virus?

DR. HAROLD K. FABER, San Francisco: Yes, if the preparation is acid.

DR. H. E. COE, Seattle: I should say that the value of pooled serum increased over that of a single donor unless the latter was of high titer.

DR. W. F. PATRICK, Portland, Ore.: Must not the serum be tested for compatibility? There is some danger in intravenous therapy, but not as much as in transfusion of blood.

DR. D. H. HOUSTON, Seattle: Regarding isolation, the accepted period is four weeks, but I believe that the disease is probably still infectious at that stage.

DR. C. L. SMITH, Seattle: What stage of the disease might be established for the administration of the serum?

DR. HAROLD K. FABER, San Francisco: The serum is indicated only in the preparalytic stage although it might be given in the early period of paralysis.

SCHÜLLER-CHRISTIAN DISEASE. Presented by DR. J. B. BILDERBACK, Portland, Ore.

The Schüller-Christian disease is one of those caused by a disturbance of the lipoid metabolism. R. S. Rowland has written a classic description of the condition in which he grouped the Gaucher, Niemann-Pick and Schüller-Christian diseases and other manifestations of faulty lipoid metabolism under the generic term xanthomatosis. Rowland, by his writings, deserves credit for calling the attention of the medical profession to this interesting disease. He had two cases of Schüller-Christian disease and collected reports on fifty-two others. He regarded them as a constitutional disorder of lipoid metabolism with pathologic lipoid storage in the reticulo-endothelial system. The outstanding symptoms of Schüller-Christian disease are defects in the bones, particularly of the skull, frequently associated with diabetes insipidus and exophthalmos.

It is generally thought that a diet low in fat, especially cholesterol, is indicated. Occasionally insulin has been given. Roentgenologists are enthusiastic about roentgen treatment, and while it is true that some conditions have been improved after roentgen or radium treatments, it is hard to conceive of great benefit, because the process is constitutional. Roentgen rays or radium may hasten the healing of the lesions of the bone, but neither stops the process going on in other parts of the body.

J. C., a white boy, 3 years of age, was admitted to Doernbecher Hospital on June 21, 1932, with symptoms of insistent thirst, frequency of urination, bulging of the right eye, constipation, prolapse of the anus and slight mental retardation. The insistent thirst and frequency of urination came on gradually over a period of about a year. On admission the child drank from 3 to 5 quarts of water a day. For about six months he had failed to progress mentally; the parents had noted that he seemed to be dull and did not respond as a normal child should. The patient's history showed that he had had frequent colds from which recovery was slow, but had had none of the diseases of childhood. He had never had cod liver oil or green vegetables.

At the time of admission, physical examination showed a pale, poorly nourished boy, resting quietly in bed, unless disturbed, at which time he would become irritable. There was a firm protuberance the size of a small walnut on the right side of the head in the temporal region. Below this were two small depressions in the skull. There was marked proptosis of the right eye. The abdomen was large, rounded and distended; the heart and lungs were normal; the liver and spleen were palpable. The liver was 6.5 cm. below the costal margin and the spleen 8 cm. below the costal margin. The skin over the back showed a slight brownish, elevated roughness. Roentgenograms of the skull showed areas of destruction of the bone, giving the appearance of being motheaten. The laboratory findings were, as a whole, not illuminating. The blood cholesterol, tested many times, varied from 90 to 300.

From June 21 to July 2, 1932, the intake of fluid ranged from 2,210 to 5,630 cc., and the urinary output, from 2,000 to 4,580 cc., a day. Starting on July 2, nasal application of powdered extract of the pituitary gland was made twice a day. Following this, there was a definite lowering of the fluid intake to an average of less than 2,000 cc. and of the urinary output to 1,500 cc. for five days. Then relapse gradually recurred. Treatment with extract of the posterior lobe of the pituitary gland was continued until Sept. 1, 1932. The intake of fluid averaged 2,500 cc., with a similar average output. The patient was discharged on Nov. 5, 1933. During this time, the condition of the skin remained about the same, and the proptosis showed no noticeable change. The soft areas in the skull became more firm. He was readmitted in December, 1932, and in February, April and June, 1933, for roentgenograms and a check-up on the condition. A noticeable increase in exophthalmos in both eyes is recorded. The nodules are larger, and the general process seems to be progressing. The intake of fluids has increased to more than 7,000 cc. a day.

DISCUSSION

DR. ARMIN REMBE, Seattle: The difference in lipoid disturbance is possibly familial, and the enlargement of the liver and the spleen possibly relates to Niemann-Pick disease. Sometimes cherry-red spots are present in the retina, if the condition is not amaurotic family idiocy.

DR. J. W. ROSENFELD, Portland, Ore.: This case is of interest to me because of an intern who has diabetes insipidus. He was first seen during infancy, with some exophthalmos and involvement of the sella turcica. This was probably a case of xanthomatosis in which recovery occurred. The intern now controls the urinary secretion by means of application of extract of the posterior lobe of the pituitary gland to the nasal membrane.

DR. C. U. MOORE, Portland, Ore.: I know of one case in which no exophthalmos is evident, but the skull gives the typical motheaten appearance.

DR. J. B. BILDERBACK, Portland, Ore.: The yellow lipoid found elsewhere in the bone probably interferes with the function of the pituitary gland.

BLOOD IN THE CEREBROSPINAL FLUID OF THE NEW-BORN: ITS RELATION TO PROGNOSIS.

Presented by DR. L. HOWARD SMITH, Portland, Ore.

The use of the terms "meningeal hemorrhage" and "intracranial injury" as synonyms has added to the confusion in evaluating the damage occurring at birth.

The frequency of bloody cerebrospinal fluid in apparently normal new-born infants after various types of labor was investigated in a series of cistern punctures on 190 new-born infants from 30 minutes to 6 days old. Bloody fluids were encountered in 16.9 per cent. None of these infants showed clinical symptoms suggestive of intracranial damage. A group of these infants has been followed, and after a period of from five to seven years we find them all normal mentally and physically. In another group of infants, all showing clinical signs of intracranial injury at the time of birth, 60 per cent had clear cerebrospinal fluids, and 40 per cent had bloody fluids. In this group 60 per cent are normal from five to seven years after birth; 30 per cent died within a day or two after birth as a result of intracranial injury, while 10 per cent are now subnormal mentally (1 showing spasticity). Of the infants in the second group (those who showed clinical symptoms of intracranial injury at the time of birth but who had a clear cerebrospinal fluid shortly after birth), only 41.61 per cent remained normal, whereas, of those with a bloody fluid, 87.5 per cent are normal.

It appears, in reviewing the two groups of cases, that the presence or absence of the clinical picture of intracranial injury at the time of birth is the all-important element in determining the end-result. The infants without clinical symptoms of intracranial injury at the time of birth, whether they had bloody fluids or not, remained normal children. Of the 6 infants who died within from twelve to seventy-two hours after birth, showing signs and symptoms of intracranial injury, 5 had clear cerebrospinal fluids on cistern puncture and only 1 had a bloody fluid. Shock is one of the chief factors in these neonatal deaths.

These findings bring up the question of the advisability of performing a cistern or lumbar puncture on new-born infants suspected of having intracranial damage. Even if the cerebrospinal fluid shows blood, what added information is there? The only indication for cistern or lumbar puncture should be to relieve the symptoms of increased pressure. Many of these new-born infants are in shock and show less than normal intracranial pressure, so that draining off of any cerebrospinal fluid, whether it is bloody or clear, is contraindicated.

DISCUSSION

DR. N. W. CLEIN, Seattle: This is an exceedingly important paper, because of the carefully controlled experiments. It is disappointing to learn that more relief of cerebral hemorrhage is not obtained by spinal or cisternal punctures. I should like to call the condition "birth pathology" instead of injury sustained at birth, for the sake of the obstetrician.

DR. HAROLD K. FABER, San Francisco: My ideas coincide with those of Dr. Smith. I agree that the same results can be obtained without interference with the spinal fluid. I think that the symptoms are sometimes caused by edema and not by hemorrhage.

DR. D. M. DAYTON, Tacoma, Wash.: At autopsy on an infant with classic symptoms of intracranial injury, there was no blood in the fluid or edema. The patient had had no fever.

DR. J. B. BILDERBACK, Portland, Ore.: What is to be done therapeutically in these cases? On what basis can one decide on puncture?

DR. N. W. CLEIN, Seattle: My opinion is that punctures should not be done except for the relief of pressure.

Book Reviews

Biologische Daten für den Kinderarzt. Volume I. By Dr. Joachim Brock. Paper. Price, 18.60 marks. Pp. 251. Berlin: Julius Springer, 1932.

Comprehensive data on the normal anatomy and physiology of infants and children have been collected in this volume, making it an especially valuable reference book for physicians dealing with children. Volume I contains the chapters on growth, including body weight and length, proportions and habitus, the skeletal system, the circulation of the blood and the digestive apparatus. The entire work has been carefully compiled, and the various sections are well organized and well indexed so that any topic can be easily located. An extensive bibliography is found at the end of each chapter. As an example of the material covered in this book, the chapter on the digestive apparatus contains a full description of the anatomy of the mouth, esophagus, stomach and bowel of the new-born, older infant and child, with the changes and measurements of various parts during growth, the motor functions of the various parts, the emptying time, detailed analyses of the secretions of the digestive organs, response to various foods, digestion and absorption of the different food elements and bacteriology and chemistry of the stools.

A Compilation of Section Reports, Recommendations and Resolutions of the Texas Conference on Child Health and Protection, 1933. Battle Creek, Mich.: W. K. Kellogg Foundation, 1933.

This publication contains the reports of the committee that worked on the Texas follow-up of the third White House Conference on Child Health and Protection. The reports were submitted at a conference held in Austin on Feb. 9, 10 and 11, 1933. There were four sections with numerous subcommittees: Section I, Medical Service; Section II, Public Health Service and Administration; Section III, Education and Training; Section IV, The Handicapped: Prevention, Maintenance and Protection. The various committees studied the conditions present in Texas and gathered data pertaining to their particular section, offering recommendations for measures that seemed indicated to promote progress in each particular field. It is the desire of the Steering Committee to place the printed report of the conference in the hands of leaders unable to attend the conference, and also to have it used by all county leaders as a guide for the promotion of child health and protection in their communities.

The Diseases of Infants and Children. By J. P. Crozier Griffith and A. Graeme Mitchell. Third edition. Pp. 1,155, with 280 figures and 73 tables. Philadelphia: W. B. Saunders Company, 1933.

The third edition of this standard work has been condensed into one volume. It is quite remarkable how the authors have been able to do this by a condensation of sentences and an elimination of material that could be spared without loss. In the reviewer's opinion the value of the book has been greatly increased. It has always been one of the most authoritative and complete of textbooks, and it is now in a character to meet the needs of the medical student or busy practitioner. There is no need to outline the contents of the book. It contains a complete résumé of pediatric practice. Its principal value lies in its thoroughness, completeness, readability and authoritative character. The references are brought well up to date, and are collected at the end of each chapter. The book is beautifully bound and printed, and the photographs are excellent and well produced.

Thérapeutique hydro-climatologique en pédiatrie. By P. Nobécourt and G. Boulanger-Pilet. Price, 22 francs. Pp. 193. Paris: Masson & Cie, 1933.

This publication is designed to assist physicians in choosing and recommending the proper European stations and spas where climatic and hydrotherapeutic measures favorable to the various disturbances of infants and children may be obtained. In part I the various diseases of children amenable to this type of treatment are discussed, with suggestions concerning the places for climate, mineral waters and baths best suited to the particular illness, age and disposition of the patient. These directions are explicit and detailed. In part II, the composition of various mineral waters is explained and their therapeutic action discussed. Part III consists of a list of the principal stations, with data on each concerning the climate, altitude, open season, facilities offered and type of illnesses for which they are especially beneficial.

Food Nutrition and Health. By E. V. McCollum and J. Ernestine Becker. Third edition. Price, $1.50. Pp. 146, with 8 tables. Baltimore: McCollum and Becker, 1933.

This is the third edition of this book, which was first published in 1925. It has been entirely rewritten and brought up to date as to recent researches in nutrition. A new chapter has been added on proteins, and these have been given more prominence then heretofore. Some excellent material has been added on suggested menus, with a thought of how best to spend the money alloted for food in the family budget. The book should be of value to lay readers, as it will enable them to discriminate between fact and fallacy in advice about foods.

Directory of Pediatric Societies

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International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.

FOREIGN

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. Leonard G. Parsons, 58, Calthorpe Road, Birmingham, England.
Secretary: Dr. W. G. Wyllie, 33, Wimpole St., W. 1, London.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Place: Cleveland. Time: June 11-15, 1934.

American Academy of Pediatrics

President: Dr. John Ruhräh, 11 E. Chase St., Baltimore.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: Cleveland. Time: June 11-12, 1934.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st. St., New York.

American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.
Place: Philadelphia. Time: Sept. 24-28, 1934.

American Pediatric Society

President: Dr. Charles A. Fife, 2104 Spruce St., Philadelphia.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.
Place: Asheville, N. C. Time: May, 1934.

Canadian Society for the Study of Diseases of Children

President: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Secretary-Treasurer: Dr. R. R. Struthers, 1414 Drummond St., Montreal.
Place: Kingston, Ontario. Time: June, 1934.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Society of Pediatric Research

President: Dr. Rustin McIntosh, College of Physicians and Surgeons, Columbia University, New York.
Secretary-Treasurer: Dr. Charles F. McKhann, Harvard Medical School, Boston.
Place: Atlantic City, N. J. Time: May, 1934.

SECTIONAL

North Pacific Pediatric Society

President: Dr. Arthur H. Gray, 1117 2d Ave., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Hugh L. Dwyer, 406, W. 34th St., Kansas City, Mo.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.

STATE

Alabama Pediatric Society

President: Dr. C. E. R. Parker, 401 S. Court St., Montgomery.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22d St., Birmingham.

Georgia Pediatric Society

President: Dr. Joseph Yampolsky, 311 Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Augusta. Time: May, 1934.

Louisiana State Pediatric Society

President: Dr. Cecil O. Lorio, 245, 3d St., Baton Rouge.
Secretary-Treasurer: Dr. Maud Loeber, Tulane University, New Orleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Adolph G. De Sanctis, 12 E. 11th St., New York.
Secretary: Dr. George M. Retan, 459 James St., Syracuse.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. W. A. Collins, 103 W. Burdick St., Kalamazoo.
Secretary: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Place: Battle Creek. Time: September, 1934.

Nebraska Pediatric Society

President: Dr. W. O. Colburn, 724 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. C. G. Weigand, 1614 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. J. Buren Sidbury, 15 N. 5th St., Wilmington.
Secretary: Dr. E. K. McLean, 121 W. 7th St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

Oklahoma State Pediatric Society

President: Dr. Clark H. Hall, 117 N. Broadway, Oklahoma City.
Secretary: Dr. M. J. Searle, 108 W. 16th St., Tulsa.

South Carolina Pediatric Society

President: Dr. J. I. Waring, 77 Rutledge Ave., Charleston.
Secretary-Treasurer: Dr. Julian P. Price, Medical Bldg., Florence.

Tennessee State Pediatric Society

President: Dr. Owen H. Wilson, 706 Church St., Nashville.
Secretary: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Place: Chattanooga. Time: April, 1934.

Texas Pediatric Society

President: Dr. Sidney R. Kaliski, Moore Bldg., San Antonio.
Secretary-Treasurer: Dr. Frank M. Martin, 321 Medical Arts Bldg., San Antonio.

Virginia Pediatric Society

President: Dr. Thomas D. Jones, Medical Arts Bldg., Second and Franklin Streets, Richmond.
Secretary: Dr. W. A. McGee, 2618 Grove Ave., Richmond.
Place: Alexandria. Time: October, 1934.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. R. C. Hood, 428 W. Pike St., Clarksburg.
Secretary: Dr. Russell C. Bond, 1325 Chapline St., Wheeling.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. A. Garvin, Carnegie Medical Bldg., Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.

Bronx Pediatric Society

President: Dr. Morris Gleich, 9 Post Ave., New York.
Secretary: Dr. Harry D. Pasachoff, 1560 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Pediatric Society

President Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn.
Secretary: Dr. Lewis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Charles Schott, 48 W. Division St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. John A. Johnston, 2799 W. Grand Blvd., Detroit.
Secretary: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Secretary: Dr. T. I. Willingham, 478 Peachtree St., N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Intermountain Pediatric Society

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. Hugh L. Dwyer, 406 W. 34th St., Kansas City.
Secretary: Dr. John Aull, 906 Grand Ave., Kansas City.

Memphis Pediatric Society

President: Dr. R. B. McCormick, 1074 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. D. Mims, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. Karl E. Kassowitz, 709 N. 11th St., Milwaukee.
Secretary: Dr. John H. Reynolds, 747 N. 27th St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Thomas A. Foster, 131 State St., Portland, Maine.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Martha Wollstein, Babies' Hospital of City of New York, New York.
Secretary: Dr. Harry Bakwin, 132 E. 71st St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.
Secretary: Dr. E. F. Robb, 1801 Lyndale Ave., S., Minneapolis.

Philadelphia Pediatric Society

President: Dr. Joseph Stokes, 159 W. Coulter St., Philadelphia.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. Henry C. Flood, 119 S. Highland Ave., Pittsburgh.
Secretary: Dr. E. R. McCluskey, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. F. Waring Lewis, Professional Bldg., Richmond, Va.
Secretary-Treasurer: Dr. A. S. Hurt, Jr., 1028 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

Rochester Pediatric Society

President: Dr. H. F. Rowley, 176 S. Goodman St., Rochester, N. Y.
Secretary: Dr. J. M. Parker, 26 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. J. A. Schoonover, Republic Bldg., Denver.
Secretary: Dr. Arthur L. Esserman, Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7 p. m.

St. Louis Pediatric Society

President: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. Albert S. McCown, 509 Olive St., Seattle.
Secretary: Dr. Frank H. Douglass, Medical-Dental Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. James E. Harvey, 60 S. Lake Ave., Pasadena, Calif.
Secretary: Dr. E. Earl Moody, 3780 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. John F. Sanders, 320 Townsend St., Lansing, Mich.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: University Hospital, Ann Arbor, Mich. Time: Nov. 23-24, 1934.

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